VOLUME 13 NUMBER 6

University Library

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION
FOR THE STUDY OF

INTERNAL SECRETIONS

EDITORS

R. G. HOSKINS, Boston

M. O. LEE, Boston H. LISSER, San Francisco

NOVEMBER-DECEMBER

1929

PUBLISHED BI-MONTHLY BY THE ASSOCIATION FOR THE STUDY OF INTERNAL SECRETIONS, SUITE 1214 WILSHIRE MEDICAL BLDG., LOS ANGELES, CALIFORNIA
ANNUAL SUBSCRIPTION, $6.00 SINGLE COPIES, $1.25

At the Menopause

The distressing symptoms that so often accompany the climacteric, but more particularly the aggravated symptoms of the artificial menopause, are frequently controlled by the administration of

LUTEIN TABLETS, H. W. & D.
LUTEIN SOLUTION AMPULES, H. W. & D.

The choice of the medication depends, of course, on the judgment of the physician as to whether oral or hypodermatic administration is indicated. Both products represent the

CORPUS LUTEUM OF THE SOW

Lutein Tablets H. W. & D. are unmodified by treatment with solvents or by exposure to temperatures above animal body heat in the drying process. All separation of extraneous matter is made by mechanical means and all drying is **in vacuo.** The unaltered **corpus luteum** should, therefore, be presented in our products and clinical experience with them should demonstrate their therapeutic activity.

Ovarian dysfunction as evidenced in dysmenorrhea and amenorrhea is also an indication for Lutein medication. Where the diagnosis of such dysfunction was well established, definite therapeutic results have been reported.

WHOLE OVARY TABLETS, H. W. & D.
OVARIAN RESIDUE TABLETS, H. W. & D.

are also offered for those who prefer, for certain indications, the use of the whole gland or of the residue remaining after corpus luteum separation.

Literature furnished on request

H. W. & D.—SPECIFY—H. W. & D.—SPECIFY—H. W. D. SPECIFY—H. W. & D.

HYNSON, WESTCOTT & DUNNING

BALTIMORE, MD.

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION FOR THE STUDY OF

INTERNAL SECRETIONS

Volume 13, Number 6 NOVEMBER-DECEMBER, 1929 Serial No. 68

THE EFFECT OF THE GROWTH PRINCIPLE OF THE HYPOPHYSIS ON THE FEMALE GENITAL TRACT

With the Report of the Hypertrophic Changes in a Case of Acromegaly

HAROLD M. TEEL, M.D.

From the Surgical Clinic of the Peter Bent Brigham Hospital

BOSTON, MASSACHUSETTS

The relation of the hypophysis to the reproductive apparatus has attracted the attention of gynecologists and clinicians since acromegaly, gigantism and the reverse states of glandular insufficiency have come to be recognized as primarily pituitary disorders. Many early experimental investigations of this problem were undertaken with the aim of clarifying the nature of the relationship. About all that came of the experiments from the point of view of genital relationships prior to the work of Smith (1, 2), Evans (3), Zondek and Aschheim (4, 5), and others, was that when the anterior lobe was largely or totally removed, either sexual infantalism or genital hypoplasia resulted, depending on the age of the experimental animal. This corresponded well with the findings in clinical hypopituitarism.

It was of course an attractive and simple deduction from these facts that if anterior lobe deficiency resulted either in failure of the genitals normally to develop or in secondary hypoplasia, excess activity would result in sexual precocity (Frühreife) or in overdevelopment of the genital system.

Though Goetsch (6), in 1916, believed that he had produced both overgrowth and accelerated sexual development in rats, by means of feeding experiments, his results have not been corroborated by others, and more recent work has demonstrated, at least in the case of mammals, the lack of effect of the anterior lobe hormones when administered by mouth.

With the introduction by Evans and his co-workers of the intraperitoneal administration of anterior lobe extract, an attack on the many problems relating to hypophysial overactivity was first made possible, and remarkable changes in the ovaries of the giant rats, produced by extracts containing the growth hormone, were promptly recognized. These organs were grossly enlarged and microscopically there was extensive luteinization of the walls of the Graafian follicles without previous rupture and expulsion of the ova. Indeed, the animals experienced oestrus only occasionally

or not at all during the period of injection. The uteri of these animals were not remarkable.

Using extracts of a similar nature, Putnam, Benedict and Teel (7) were able to confirm the findings in rats, but when dogs were used as the experimental subjects quite different results were obtained. In these animals, overgrowth was also produced, but the ovaries, while several times the normal size, contained no lutein tissue whatsoever. The increased size was largely due to increase in stroma with some enlarged and numerous degenerating follicles. The uterus and vagina, however, had become tremendous in contrast to the slight change produced in rats. (Fig. 1).

With the evidence produced by Smith, by Zondek and Aschheim, and by Evans and Simpson (8), which clearly demonstrated the existence of a separate gonad-stimulating substance in the anterior lobe, the interpretation of the effects from growth-promoting extracts became more difficult.

Evans and his collaborators have shown that the alkaline extracts which were used for promoting growth contain largely growth principle, but also may contain varying small amounts of the more recently demonstrated "hypophyseal sex hormone." That the great enlargement, predominantly of the uterus and vagina, in dogs treated with neutralized alkaline extracts of the anterior lobe, may be due either to the growth-promoting principle which these extracts contain or to contamination with a small amount of the so-called "sex hormone" of the hypophysis, must be recognized as alternative possibilities. While the striking effect of the gonad-stimulating principle is not to be denied, it would appear that the growth principle by itself may cause great enlargement of the genital system.

Though the laboratory will always remain our chief source of precise data regarding such complicated subjects, suggestive or corroborative information may often be secured from the clinic. It has already been shown by papers from this clinic [Bailey and Davidoff (9), Bailey and Cushing (10)] that the adenomas associated with clinical hyperpituitarism (acromegaly) are composed of acidophilic cells; that the more common adenomas causing the reverse state of acquired hypopituitarism are composed of cells of the chromophobe type; that true basophilic adenomas are unknown. Whereas the growth-promoting substance is supposed to be confined to the acidophilic cells, the experiments of Smith and of Engle (11) tend definitely to localize the gonad-stimulating substance in the basophilic cells, and it is natural to assume, therefore, that a female patient with an acidophilic adenoma and marked acromegaly in the absence of amenorrhoea would be receiving an excess only of the growth-promoting principle of the gland, the sex hormone remaining unaffected.

Complete postmortem examinations of patients with acromegaly are not common, and in the cases reported scant attention has been given to the condition of the pelvic organs. This fact was emphasized by Cushing and Davidoff (12), who found in the literature only four cases in which

the female genital system was at all adequately described, and in these it appeared that there was nothing sufficiently striking to attract notice. The hyperplasia of the genital tract appears to have been wholly overlooked,

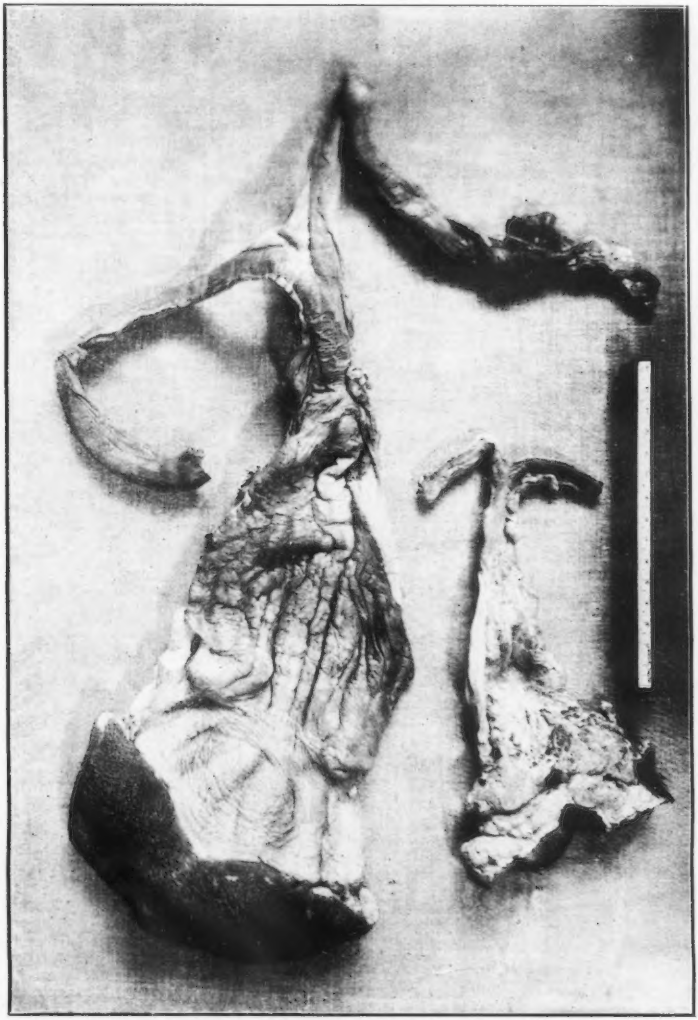

Fig. 1.—The uterus and vagina of an acromegalic dog (left) which had been treated for 14 months with extracts containing the growth-promoting principle of the anterior hypophysis. The uterus and vagina of the littermate control are shown on the right for comparison. (Putnam, Benedict and Teel.)

and the notes on the ovaries in general called attention merely to slight enlargement, increased stroma, frequent small cysts and occasional corpora atretica.

They were able to add a description of the ovaries in two more cases. The first was a woman of 26 who had been married three years and had subsequently become amenorrhoeic. The report on the pelvic organs follows:

"The right ovary measures about 4 cm. in length and about 2 cm. in width. On section there are numerous small cystic areas. The left ovary measures about 6 cm. in diameter. On section the greater part of this is found to be made up of smooth-walled cysts containing perfectly clear colorless fluid. The ovarian tissue has been compressed and spread out and measures only 4 mm. in thickness. The uterus is 6 cm. in length and about 3 cm. in width. It is rather dark red in color. The mucous membrane is pale and of a glossy smoothness. The cervix is corrugated."

Microscopic examination revealed four large Graafian follicles, one of which might have been regarded as cystic. These follicles contained apparently normal ova. No corpora atretica and no traces of lutein tissue were seen; and only a single primordial ovum was found.

Cushing and Davidoff's second case concerned a woman who died at the age of 52 with acromegaly of long standing. The catamenia had continued for many years after the acromegaly had become apparent, the menopause having occurred at 40, twelve years prior to her death. The

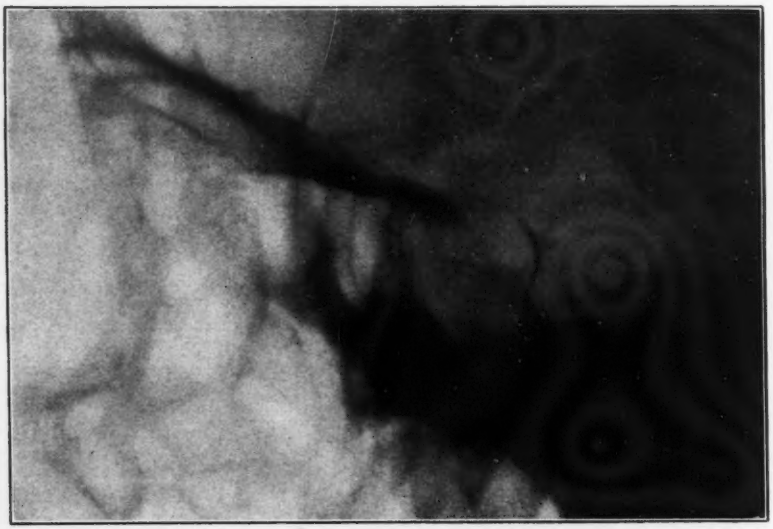

Fig. 2.—Skiagram of the skull from the case presented, showing the typically ballooned sella.

ovaries were reported as small and fibrous, and no microscopic report was made. One could have hoped for but little information from the specimen, since it was obtained twelve years after the menopause.

Further light on this subject has been shed by the following case:

Surgical No. 33265. Advanced acromegaly of seven years known duration in a single middle-aged woman without interruption of catamenia. Moderate enlargement of sella but no neighborhood symptoms. Menorrhagia, and hysterectomy for supposed fibroid. Findings: marked diffuse hypertrophy of uterus and entire genital tract.

Feb. 11, 1929. First admission of Miss A. B. C., aged 49, referred by Dr. H. C. Gordonier of Troy, New York, for advice and treatment of her acromegaly.

History. The family history was irrelevant apart from the statement of the patient that she believed that her younger brother was developing changes in his features similar to her own. The general health of the patient had been excellent until 1922 when, at the age of 42, symptoms referable to her acromegaly first appeared. The initial symptoms were excessive fatigability and drowsiness. Two years later, in 1924, the sleepiness had become so marked as to interfere with her work. For this reason she first consulted Dr. Gordonier, who recognized the presence of early acromegaly, the manifestations of which had subsequently progressed until, according to the patient's statement, she had become unrecognizable by some of her former acquaintances.

The appetite had been voracious and she had gained about 40 pounds during the course of her malady. Except for slight diminution of visual acuity in the past three years, there had been no subjective neighborhood symptoms. Her catamenia, which had always been regular and normal, continued, without interruption, in spite of the advancing malady. For a year previous to admission, however, the flow had been somewhat scant and of offensive odor. There had been no discharge between periods.

Examination. This showed a well nourished woman of middle age with typical features of well advanced acromegaly, in the absence of neighborhood symptoms. The optic discs were normal and there were no constrictions of the temporal fields of vision. The x-ray films revealed a definite expansion of the sella outlines (Fig. 2) and well marked acromegalic changes in the skeleton elsewhere. The average of several determinations of the basal metabolic rate was +23 per cent and the specific dynamic action to protein, as shown by the response to a test meal of ground beef, gave a rise from the fasting rate of 23 to 41 per cent in one hour. There was no vaginal examination nor any special note made of the patient's pelvic organs.

The diagnosis of pituitary adenoma with acromegaly was unmistakable, and because of the absence of any chiasmal involvement x-ray treatment was advised. Four x-ray treatments were given,* directed through the right and left temporal regions alternately, on Feb. 20, 21, 26, and 27th, and when the patient was discharged a few days later, definite improvement was already apparent. The drowsiness had practically disappeared, the energy and alertness had greatly increased and there was already appreciable diminution in the boggy tissues so that her gloves and shoes had become noticeably loose. The patient was discharged too soon for the change to be reflected in loss of weight as it did during the second stay in the hospital mentioned below. At the time of her discharge on March 1, 1929, the basal metabolic rate had dropped to +10 per cent.

Subsequent note. The patient wrote April 2, 1929, to say, that her friends remarked on the change in her appearance and that she was subjectively much improved. She wrote a month later stating that her last period was ten days late, and that when it did come there was severe menorrhagia for two weeks. A local doctor found on examination "a fibroid of the uterus as large as a grapefruit," and advised radium or return to the hospital for treatment. A subsequent period which began June 5th was of normal character and duration.

Readmission. June 11, 1929. The patient was admitted to the surgical service with the history of menorrhagia and with the diagnosis of a uterine fibroid.

Pelvic examination. The external genitalia were larger, more vascular and thickened than normal. The labia were particularly redundant and there seemed to be a great deal of vascular stasis. The vagina was large and the vaults were particularly deep. The cervix was large and bluish and the easily palpable uterus was symmetrical, firm in consistency, and about the size of a small grapefruit. There were no masses in the adnexal regions. *Diagnosis:* uterine fibroid.

On June 21st and 22nd while awaiting her pelvic operation two more radiation treatments were directed to the hypophysis. The patient began to lose weight immediately and the large lips and nose as well as the hands and feet visibly diminished in size from day to day. She remarked one day that she was able to see the tendons and bones of her hands for the first time in years.

Operation. June 24, 1929. (Dr. Francis C. Newton) ***Hysterectomy and bilateral salpingo-oophrectomy.***

*50% of an erythema dose. 185 Kv. 40 cm. target skin distance. ½ mm. copper plus 1 mm. aluminum, filter. Portals—10 x 10 cm.

Fig. 3.—The uterus with adnexa of the case presented showing the marked diffuse hypertrophy of the uterine masculature.

Under ether anaesthesia a midline incision was made and on lifting the bowel and omentum from the pelvis a markedly hypertrophied and congested genital tract was exposed. The uterine and ovarian vessels were dilated and tortuous. The uterus was symmetrically enlarged, congested and freely movable. Posteriorly, the pouch of Douglass was remarkably deep and the posterior vaginal wall with its covering peritoneum was thrown into great folds. The broad ligaments were congested, thick and of meaty consistency. Below the outer ends of both tubes there were a few small parovarian cysts. The ovaries were of good size although perhaps no larger than are often seen in non-acromegalic women. The left ovary was bound to the posterior aspect of the uterus and broad ligament by a number of old adhesions. There was a small hemorrhagic cyst in the right ovary.

The uterus, both tubes and ovaries were removed on the assumption that the uterine enlargement was due to an intramural fibroid.

Subsequent notes. The patient made an excellent surgical recovery. Doubtless as a result of the preoperative x-ray treatments the subsidence in the size of the extremities progressed with a total loss of weight amounting in all to 7.4 kgm. by the time of her discharge, *July 13, 1929.*

Pathological description. The gross specimen weighs 510 grams. It consists of a symmetrically enlarged uterus, with both tubes and ovaries. Below the outer end of either tube are a number of small parovarian cysts (Fig. 3).

The uterus measures 12x11x7 cm. and is of a uniform, somewhat soft consistency. On section the cut surface bulges slightly; the wall measures 4½ cm. in thickness, and appears to be composed of rather coarse bundles of interlacing fibres. No gross tumor mass is found. The endometrium is somewhat thickened and shows numerous fairly firm elastic polyps which appear to be completely covered with epithelium.

The tubes are not remarkable although they are of large size and hyperaemic.

The right ovary measures 4½x2½x2½ cm. and contains a cyst 2½ cm. in diameter which is filled with blood-stained fluid.

The left ovary measures 3½x2½x1½ cm. The surface is markedly scarred although the fluctuant consistency suggests that internally it is cystic.

Microscopic examination. The uterus shows a very thick wall composed of normally arranged smooth muscle bundles with no suggestion of leiomyomatous formation or fibrosis. The musculature, while hypertrophied, appears entirely normal. The endometrium shows hyperplasia with abundant loose textured stroma and a moderate increase in the number of endometrial glands. Section of a polyp shows it to be of the usual mucous variety.

The tubes show little change apart from numerous dilated thin-walled blood-vessels.

The right ovary shows on microscopic examination a corpus luteum with hemorrhage into the central portion, the hemorrhage being surrounded by several layers of atypical lutein cells. The left ovary shows numerous corpora albicantia, several follicular cysts and a rather dense ovarian stroma.

Pathological diagnosis. Hypertrophy of the uterus, hyperplasia of the endometrium with mucos polyps, and simple cysts of the ovaries.

COMMENT

The case presented is of particular interest for two reasons. First, although the patient had had advancing acromegaly for seven years, with an enlarged sella, and was 49 years of age, the catamenia had been remarkably regular and of normal character. Second, the changes in the genital tract resembled in many respects those found in dogs with experimentally produced acromegaly—namely, marked hyperplasia of the whole genital tract without striking histological changes in the ovary.

We may assume in this case that the acromegaly was an expression of an eosinophilic adenoma which had in no way affected the function of the

basophilic cells; that the genital hyperplasia therefore may be looked upon as a direct effect of the activity of the eosinophilic adenoma.

The marked similarity between the genital system in this case, in which there was presumably an increased secretion of the growth-promoting substance alone, and the genital hyperplasia induced experimentally in dogs by means of alkaline extracts of the anterior lobe which certainly contain predominantly growth-promoting substance, would indicate that the growth-promoting principle may produce marked hyperplasia of the genital tract in the female.

The hyperplasia may be regarded merely as an hitherto unrecorded expression of the visceral splanchnomegaly that characterizes the disease.

BIBLIOGRAPHY

1. Smith, P. E.: J. A. M. A. **88:** 158. 1927.
2. Smith, P. E. and E. T. Engle: Am. J. Anat. **40:** 159. 1927.
3. Evans, H. M.: Harvey Lectures, 1924. Lippincott, Phila.
4. Zondek, B. and S. Aschheim: Ztschr. f. Geburtsh. u. Gynek. **90:** 370. 1926.
5. Zondek, B. and S. Aschheim: Klin. Wchnschr. **7:** 8. 1928.
6. Goetsch, E.: Bull. Johns Hopkins Hosp. **27:** 29. 1916.
7. Putnam, T. J., E. B. Benedict and H. M. Teel: Arch. Surg. **18:** 1708. 1929.
8. Evans, H. M. and M. E. Simpson: J. A. M. A. **91:** 1337. 1928.
9. Bailey, P. and L. M. Davidoff: Am. J. Pathology. **1:** 185. 1925.
10. Bailey, P. and H. Cushing: Am. J. Path. **4:** 545. 1928.
11. Engle, E. T.: Am. J. Physiol. **88:** 101. 1929.
12. Cushing, H. and L. M. Davidoff: Monogr. Rockefeller Inst. M. Research, No. 22. 1927.

PITUITARY TUMOR ASSOCIATED WITH GYNECOMASTIA

R. C. MOEHLIG, M.D.
Department of Internal Medicine, Harper Hospital
DETROIT, MICHIGAN

The following case of pituitary tumor illustrates what is already so well known, namely, that the pituitary gland influences the sex development of the individual. This case illustrates how certain types of pituitary tumor may produce an inversion of the sex characteristics.

The patient, a man of 52 years of age, referred by Dr. L. Adler, was admitted to Harper Hospital on May 21st, 1929, with a *history* that for about a year he had had vertigo and headache in the frontal region and impotency for the last two years. He had noticed that during the past two years his breasts were increasing in size and were taking on so-called female characteristics. Vertigo had increased over the period of the last year and in the last month previous to admission it had become very much worse. The headaches likewise increased.

Fig. 1 Photograph of patient described in text.

There was no complaint about vision. Four weeks prior to admission he began to notice a gradual loss of the use of the right arm and drooping of the right corner of the mouth. His speech became so much affected that he was able to speak only in monosyllables. The impotency had developed gradually, beginning two years ago.

Physical examination revealed a heavy set man weighing about 170 pounds and 5½ feet in height. The reaction of the pupils was normal and there was no nystagmus. The right angle of the mouth drooped to a marked degree. There was marked pharyngitis present and the tonsils were very large. An adenomatous

goiter involving both lobes of the thyroid was present. The breasts were definitely of female type and were very pendulous. The pigment of the areola and nipple showed definite female characteristics. He had a female distribution of the pubic hair. The axillary hair was rather sparse. The development of the hair on the upper lip was good. The patellar reflexes were diminished on the right, normal on the left. No Babinsky sign could be elicited on either side. There was spasticity and increased reflexes of the right arm. The testicles were very small, about one-half normal size. There had been involuntary urination for about one month. The temperature was normal, pulse 84, blood pressure 150/70.

Laboratory Findings: Microscopic examination of the urine revealed many pus cells. The blood nitrogen was 54.5 mgm. per 100 cc. blood; the fasting blood sugar was 0.111 per cent. Blood examinations showed: W. B. C., 10,000; P. M. N., 69 per cent; S. M., 20 per cent; L. M., 11 per cent; R. B. C., 4,860,000; Hb., 80 per cent.

Examination of the spinal fluid gave normal findings throughout.

The blood Wassermann reaction was negative on two occasions.

The basal metabolic rate was minus 15 per cent. A glucose tolerance test was made. The fasting specimen showed 0.083 per cent; at ¾ hour, 0.117 per cent; 1½ hour, 0.143 per cent; 2½ hours, 0.111 per cent.

X-ray examination of the skull revealed some thickening of the inner table in the right frontal region. "The sella turcica is enlarged and there is erosion of

Fig. 2. Under surface of the brain, showing pituitary tumor encroaching upon the left cerebrum.

the floor and dorsum sella. Conclusions: The erosion of the floor posteriorly and the changes in the sella would indicate a pituitary tumor."

Ophthalmoscopic examination revealed atrophy of both optic discs. The nerves were whitish blue and the outlines of the discs showed some edema with veins fuller than normal and slightly tortuous, indicating pressure. The tension was normal. The examiner was "unable to get vision or perimetric fields on account of the patient's mental condition and lack of coöperation."

On May 27th, ascending lipiodol, 7½ cc. was injected into the spinal canal. X-ray examination of the skull following this injection showed the lipiodol in the fourth ventricle in the cisterna magnum. "There were a few droplets which apparently had passed into the lateral ventricles. We do not believe, however, that the lack of filling with lipiodol could be interpreted as indicating an obstructive lesion between the third and lateral ventricles. The distortion of the sella turcica previously described is again evident."

Two days after the injection of the lipiodol, during the afternoon, the patient's temperature rose to 101.6°, pulse to 130, and respirations to 22. On May 30th, 1929, the axillary temperature was 101°, the pulse 148, and respirations increased to 48, and the patient went into coma. The respirations became very

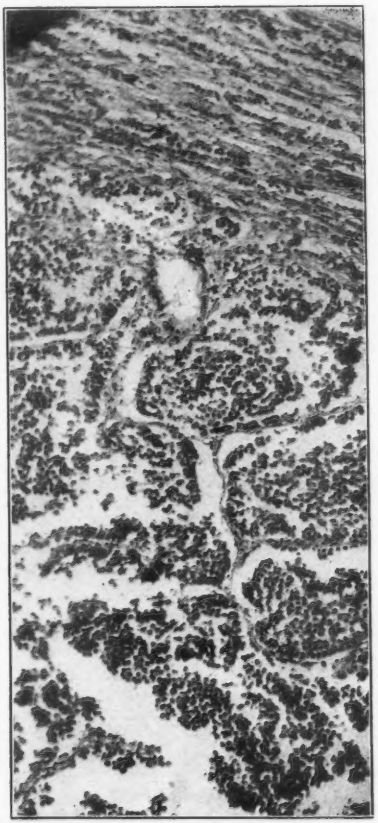

Fig. 3. Photomicrograph of a section of the tumor.

rapid and shallow and there was free diaphoresis present. On May 31st, the patient was still comatose with pulse 160 to 170 and respirations 48. He expired on May 31st, 1929, at 11:45 p. m.

The *post mortem* examination was limited to the head. This is to be regretted in view of the fact that it would have been interesting to study suprarenals and testicles.

Report of the autopsy is as follows: "The subject is an extremely obese, middle-aged male. The distribution of fat is strikingly that of a female. The breasts are very large and pendulous. The pubic hair line is straight across, just above the pubis. The axillary hair is scanty. The testicles are small.

"On opening the dura, globules of oleaginous material were seen to be present in the spinal fluid. (This was lipiodol previously injected intrathecally.) The pia arachnoid is thick and edematous and the blood vessels are engorged. On lifting the frontal lobes a large tumor is seen in the sella turcica which has been greatly enlarged. The posterior clinoid process of the sella is not present on the left side, where the tumor is mostly asymmetrical. The tumor has stretched the optic chiasm so that it is like a small band ¾ inch long extending between the optic nerves. The tumor is about 1¼ inches long and pear shaped, with the small point attached to the region of the infundibulum. The tumor is solid and has the consistency of a testicle."

The *pathological diagnosis* was: *"Pituitary adenoma."*

Microscopical examination: "The tumor consists of a rather histoid mass of cells of uniform character arranged within a delicate connective tissue stroma carrying the large thin walled veins. There is a definite tendency to alveolar

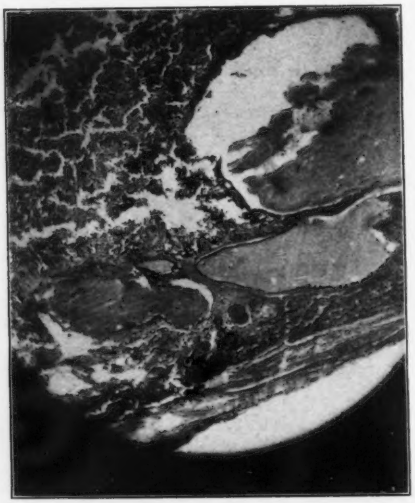

Fig. 4. Photograph showing the atypical cells in the capsule surrounding the pars intermedia.

and nest-like arrangement, although in places this is lost and the structure becomes uniform. The atypical cells are invading the capsule of the tumor and surround the pars intermedia, which appears normal as to follicle structure and colloid material.

The individual cells in the hematoxylin eosin stain closely resembles a plasma cell in staining qualities, size and nuclear structure. The nucleus, however, is not uniformly eccentric, but is more centrally placed.

With the ethyl-violet, orange G. stain the cells are found to be uniformly of the chromophobe type.

Diagnosis: Chromophobe adenoma of the hypophysis." P. F. Morse, M.D.

SUMMARY

The case is reported of a man of 52 in whom a gradually developed impotence, feminine pubic hair distribution and gynecomastia are evident. A skiagram gave evidence of a large pituitary tumor. This at autopsy was found to be a chromophobe adenoma of the hypophysis.

DYSTROPHIA ADIPOSOGENITALIS, WITH ATYPICAL RETINITIS PIGMENTOSA, MENTAL DEFICIENCY, AND POLYDACTYLISM

(The Laurence-Moon-Biedl Syndrome)

Report of a Case.

H. LISSER, A.B., M.D.
SAN FRANCISCO

Laurence and Moon (1) in 1866 reported a family group of four of eight brothers and sisters, who showed retinitis pigmentosa, adiposity, genital dystrophy and mental deficiency; three of these likewise showed imperfections of bony and muscular development leading to defective gait; there was no sign of rickets, of scrofula, nor of syphilis. "The author recognized that the retinal changes were but part of a general developmental failure and that, especially in view of the mental condition, these persons could be, not inaptly, compared to cretins" (quoted from article by Solis-Cohen and Weiss).

Biedl (2) in 1922 and Raab in 1924 (3) report another family of six living boys and girls of healthy parents, two of whom (a brother and a sister) showed atypical retinitis pigmentosa, adiposity, genital dystrophy, polydactylism and mental deficiency. Two others of the family who died in infancy showed polydactylism. Assuming that these might have developed the full syndrome had they lived, Solis-Cohen and Weiss comment upon the remarkable parallel of four healthy and four affected children in this group, in that of Laurence and Moon, and in the group recently reported by themselves.

Biedl refers to an observation in the ophthalmalogical literature by Bardet (1920), who describes a syndrome composed of infantile adiposity, polydactylism and retinitis pigmentosa, and reported one case. De Schweinitz (4) mentions three cases in which he noted the association of pigmentary degeneration of the retina with pituitary diseases and polydactylism. Engelbach, in a personal communication to Solis-Cohen, states that he has seen two cases of this syndrome.

Solis-Cohen and Weiss in 1925 (5) report four of eight brothers and sisters of Italian parentage who exhibited marked adiposity with mental deficiency, genital dystrophy, and atypical retinitis pigmentosa (with diminution of vision); two of the abnormal children also showed polydactylism. The fat distribution was largely of the girdle, mons and mammary type. No anomaly of osseous development was found as far as the sella turcica and sella region were concerned. Sugar-tolerance tests did not indicate pituitary disease; basal metabolism was below normal in three of the children; Wassermann tests were negative in all the children and the

*Presented at the meeting of The Pacific Coast Oto-Ophthalmalogical Society, Salt Lake City, July 1-2, 1929.

parents. The thyroid glands appeared to be normal. The poor vision was first noticed at 10, 13, 15 and 16 years respectively. Height, temperature, pulse, respiration, urinalysis, blood pressure and blood count were uniformly normal.

The literature up to April, 1925, has contained reports of twenty cases of this extraordinary syndrome. It is possible that an exhaustive search might uncover a few more instances. It would seem justifiable to regard this distinctive clinical complex as a pathological entity. Solis-Cohen and Weiss, who have had opportunity to reflect on the theories of Biedl and Raab and others, reserve their opinion and await the progress of future research respecting a congenital pituitary deficiency or a congenital defect of trophic centers in the hypothalamus as the pathogenetic factor in this disease.

It so happened that one morning an orthopedic colleague requested me to see an obese girl, whose osteomyelitis he was treating. On the way up to the ward he added that the little patient was almost blind. This elicited my interest and I was already picturing the possibility of a chromophobe adenoma of the hypophysis. Soon after examination was begun this suspicion was abandoned and in its place there came to my mind the rare syndrome described in the preceding paragraphs. The occasion for this change of front was the finding of supernumerary toes. I immediately went in search of the university ophthalmalogist and the picture was completed when he reported the fundi as characteristic of atypical retinitis pigmentosa.

CASE REPORT

In view of the great rarity of this extraordinary syndrome the following case is herewith recorded:

I. R., aged 8, Spanish, U. C. H., Nos. 48189, 48760, and 49343.

Inquiry into the family history revealed that one maternal uncle had six fingers on one hand. The immediate family consisted of seven brothers and sisters, two of whom died at thirteen and eighteen months respectively. The brother who died at eighteen months of age had six toes on each foot. The three living sisters and one brother of the patient, ranging in age from four months to seven years, seemed to be normal from all accounts, though we had no opportunity of examining them. The family resided at a considerable distance from San Francisco.

It was stated that the patient underwent a normal birth and an uneventful infancy except for two attacks of pneumonia, two months apart, at around one year of age. It was related "that the baby was stuporous for seven days during the second attack." It was shortly after this that the mother first noticed defective vision, a "cross-eyed" appearance, and the first evidence of mental retardation. The girl had always been stout. Otherwise the past history was entirely negative. A physician had examined the eyes when the girl was six years old and stated that "the nerves were involved."

When the patient was seven and one half years of age an abscess appeared at the right shoulder. It was this disturbance that brought the patient to the hospital. X-ray showed an osteomyelitis of the right humerus which was appropriately treated. No further mention will be made of this since it has no relation to the syndrome to be described.

As may be noted in the photograph (Fig. 1), the patient was quite obese, the adiposity being of the so-called "pituitary type." Fig. 2 reveals the supernumerary toes. It was noticed that she walked with difficulty, bumping into things, and that she followed a person apparently by sound rather than sight;

when fed she did not open her mouth until food touched her lips; she made no attempt to look forward toward the spoken voice; she never uttered any sentences, only an occasional Spanish word. It was difficult to estimate her mental age since the child did not understand English, but our psychiatrist, Doctor Olga Bridgman, concluded that her mental age was probably less than two years, a retardation of six years; probable idiocy, necessitating permanent custodial care. The child was cleanly in her habits and had perfect sphincter control. Her inability to see made her unnecessarily fearful so that she yelled loudly when any attempt was made to examine her.

Figure 1

Roentgenogram of her chest did not reveal any thymus enlargement; the heart and lungs appeared normal. Roentgenograms were taken to determine her bone age and it was concluded that ossification lay between seven and nine years of age; nearer seven. Roentgenogram of the skull revealed no abnormality; the sella turcica was normal. Routine examinations of the urine and blood were normal. The Wassermann test was negative. Her blood-serum calcium was 10.4 mgm. per 100 cc. (normal). Glucose tolerance gave the following values: Fasting, .090 per cent; ½ hour after glucose, .170 per cent; 1½ hours after glucose, .105 per cent.

Neurological examination was negative except for the second, third and seventh cranial nerves. The latter was thought involved because of slight facial asymmetry.

I am indebted to Doctors Cordes and Horner for the following report of her

eyes: "Left eye is divergent and child looks habitually to the left. She is aware of a flashlight when brought near to her, although she does not follow it with her eyes (light perception only). The eyes make typical searching nystagmoid movements. Under anesthetic and dilatation the media are clear. The right disc is somewhat pale. Its edges are sharp. The fundus vessels are slightly smaller than normal. Some of them bear whitish streaks along their course across the disc. The retina is unusual. A grayish reflex or sheen is quite remarkable. Myriads of very small grayish dots appear throughout the retina except in the macular area. The dots are not clean cut but are round and of the same color, although size may vary from minute to the size of a primary retinal vessel. They are in no place surrounded by pigment. Throughout the fundus but particularly in periphery and mid-periphery are occasional elongated spider leg shaped threads of pigment. They occur often along vessels and when in

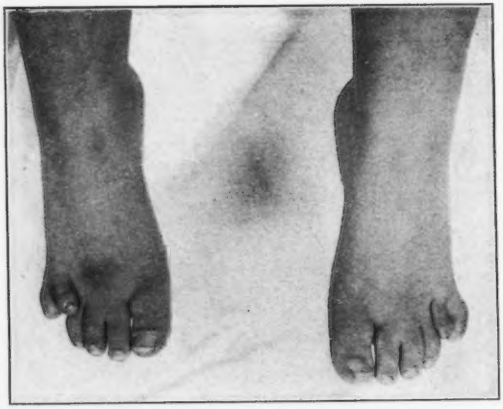

Figure 2

contact cover the vessel (that is, anterior to them). They branch occasionally but are usually in strands. The macular area is clear. Similar findings were noted in the right eye.

Discussion: This is a retinitis associated with retinal atrophy, blindness, whitish dots and pigment proliferation. The lesions are in retina and *not* choroid (i. e., not choroiditis). The whitish dots belong to those of retinitis punctata albiscens but the pigment is not punctate but strand-like.

Diagnosis: The case is one of retinitis sharing features of atypical retinitis pigmentosa and a closely associated type retinitis punctata albiscens.

The *prognosis* is absolutely bad. No improvement can be expected and vision may even get worse.

Addendum: Since the above report was written two articles have appeared, one by Beck in a recent issue of "Endocrinology," and another in the German journal, "Endokrinologie," recording other instances of this syndrome.

CONCLUSION

A case of the extremely rare Laurence-Moon-Biedl Syndrome has been recorded. The writer has no original theories as to the etiology of this bizarre symptom complex and nothing to add to the excellent article of Solis-Cohen and Weiss, to which the reader is referred for further details.

BIBLIOGRAPHY

1. Laurence, J. Z. and R. C. Moon: Brit. Ophth. Rev. **2**: 32. 1866.
2 Biedl, A.: Deutsch med. Wchnschr. **48**: 1630. 1922.
3. Raab, W.: Wien, Arch. f. inn. Med. **7**: 443. 1924.
4. de Schweinitz, G. E.: Trans. Am. Ophth. Soc. **43**. 1923.
5. Solis-Cohen, S. and E. Weiss: Am. J. Med. Sc. **169**: 489. 1925.

THE EFFECT OF ADRENALINE ON THE HEART OF THE CHICK EMBRYO

DR. TSUNEO MATSUMORI
NAGASAKI, JAPAN

INTRODUCTION

The influence of various medicaments upon the heart has been widely studied. The earlier experiments for the most part dealt with the hearts of adult animals. So far as we are aware few similar studies have been made on the embryonic heart. It seemed desirable, therefore, to make such a study, using adrenaline as the test substance. During the course of our studies Doctor Tuji of Kioto published the results of a similar investigation which were not, however, entirely in accordance with ours.

We have studied the action of adrenaline on the embryonic chick heart and on strip preparations of it at different stages of development. The hearts were removed, kept in warm Ringer's solution and tested in the same solution.

The first appearance of automatic movements in the embryonic chick heart: Since the time of Aristotle the beat of the embryonic chick heart has frequently been observed. The period at which this is first evident, however, has been quite differently reported by different observers. Harvey noted that the heart beat could be detected with careful observation at the end of the third day and easily on the fourth day of embryonic development. Aldrovandus found two beating structures in the 4-day embryo, one in the heart and one in the liver. Later observers have noted the first appearance of heart beats in the chick embryo at the following ages (in hours).

Haller	45
Prevost and Dumas	36-39
v. Baer	48
Carpenter	38-40
Wernicke	46
Laborde and Laveran	26
Preyer	36
Ohara	33-34
Fujii	45

This last author saw no case of appearance of beats earlier than the 40th hour. In our researches the heart beat has been seen in one experimental case as early as the 28th hour, but in most cases only after 33 to 35 hours of incubation. As we see, then, the time of the first beating occurs at a variable period. Some of the conditioning factors are temperature of incubation, kind of egg, climate, etc. Indeed, in our single observa-

tion of a heart beating at the 28th hour the time was summer and development had probably begun already before the egg was put into the incubator. Oliviero Olivo noted that the first heart beat ordinarily occurs when nine somites have been differentiated. He found that at this time no nerve fibers have yet penetrated the heart. Our observations confirm the fact that the first heart beat never precedes the appearance of the 9th somite.

It is to be noted that if, in a given experiment, no heart beat is to be seen with the embryo in situ it should be removed to warm Ringer's solution. Ordinarily, the extirpated heart begins to beat within a few minutes but it persists not more than twenty minutes. The heart beat persists especially long in the third and fourth days of incubation, hence, this age is favorable for experimental purposes. The better activity of the isolated heart as compared with that in situ is perhaps to be ascribed to a depressing influence of body metabolites as previously emphasized by Ohara. Our own observations have been made only on extirpated hearts.

Heart strip preparations: According to Kuliabko in the normal heart cycle arrest occurs at different times in different parts: First in the left ventricle, then in the right ventricle and in both auricles and last at the mouths of the great veins in the right auricle. The next beat courses over the heart in the same order. Fano observed movements in small bits of isolated heart tissue of 2-3 day embryos. He determined that the tissue from around the mouths of the great veins beat with normal frequency after removal, whereas, other parts came to a standstill. Later, these parts began to beat but at a diminished rate. Fano ascribed these differences to the fact that the auricle has strongly developed automoticity and weak irritability, whereas, in the ventricle the conditions are reversed. This observation we have confirmed. The frequency diminishes as a rule after isolation of the strips.

METHODS

Material and incubation: The eggs were obtained fresh from a nearby poultry farm. They were incubated at 38° C. Ventilation was carefully watched. Incubation was reckoned from the time of placing the egg in the incubator.

Heart extirpation: The embryo was removed through a window in the shell made by scissors and placed in Ringer's solution at 38-39°. Either the whole heart was used for subsequent experiments or heart strips were prepared.

Heart strips: The heart of a three-day embryo consists of merely a small tube from which only two strips can be prepared, namely, from the region of the mouths of the great veins and from the chamber region. This is true also of the four-day embryo. From the fifth to the seventh day, however, a third preparation can be made from the tip of the heart.

Apparatus: A ten centimeter container is half filled with Ringer's solution. This is then placed in a larger container filled with warm water.

The temperature of the Ringer's solution is maintained at 37° C. by the addition of warm water to the outer container as needed. The Ringer's solution is copiously supplied with warm oxygen. To avoid any injurious effect of the oxygen blast it is directed by means of a small glass plate which serves as a dividing wall between the test objects. The heart or strip preparation is observed through a microscope.

Procedures: Upon introduction into the Ringer's solution the heart preparation at first beats irregularly. This is succeeded by a regular rate whereupon the experimentation can begin. Adrenalin is introduced by drops along the side of the container as far as possible from the preparation. The frequency of beats is then determined at the end of 30 seconds and at intervals to the end of 10 minutes. Pieces that beat irregularly are discarded. The adrenalin chloride of the Sankio Compound, supplied in ampules for injection, is used. This is preserved with chloretone in one-half per cent concentration. The adrenalin is diluted ten-fold with distilled water warmed to 37° C. and introduced with a fine pipette. Fifty drops of this solution make 1 cc. and if 1 drop is added to 5 cc. of Ringer's solution a concentration of 0.0000392 per cent of adrenalin is secured. Either Locke's or Ringer's solution can be used as nutrient medium. We have employed a mixture worked out by Dr. Okuda, consisting of:

Sodium bicarbonate -	0.01%
Potassium chloride - -	0.01%
Calcium chloride - -	0.02%
Sodium chloride - - -	0.90%

III. EXPERIMENTAL RESULTS

A—The influence of adrenalin on the extirpated heart at different stages of development.

1. *At 29-40 hour stage:* At this stage adrenalin causes a clean cut increase in frequency and in strength of contraction. The effect is short lasting. The increase in frequency ranges from 1:1.09 to 1:1.92, the average being 1:1.49 (See table 1).

2. *At 41-50 hour stage:* The reaction at this stage is similar to that just described. The relative frequency before and after adrenalin administration varies between 1:1.11 and 1:1.94, averaging 1:1.43 (See table 2).

3. *At 51-60 hour stage:* The effect is, with one exception, the same, by and large, as above. The effect comes on more slowly, however, and persists longer than in the younger preparations. The range at this stage is from 1:1.11 to 1:1.60, the average being 1:1.46 (See table 3).

4. *At 61-70 hour stage:* The effect on frequency is somewhat less and the duration is somewhat more prolonged. The range is from 1:1.04 to 1:1.40, averaging 1:1.19 (Table 4).

5. *At 71-80 hour stage:* Here there is an increased effect and longer persistence. The range is 1:1.10 to 1:1.58, averaging 1:1.31 (Table 5).

6. *At 81-90 hour stage:* The accelerating effect is greater here than in the foregoing. The range is from 1:1.26 to 1:1.72, the average being 1:1.48 (Table 6).

7. *At 91-100 hour stage:* At this stage we have observed the most marked effect of adrenaline, as regards both frequency and contraction. The range is from 1:1.13 to 1:2.22, averaging 1:1.53 (Table 8).

8. *At 101-110 hour stage:* The effect of adrenaline is still evident but weaker. The increase in frequency is comparable to that of the earlier stages and the range is from 1:1.24 to 1:1.65, averaging 1:1.47.

9. *At 111-130 hour stage:* The effect is still weaker, being comparable to that of the 71 to 80 hour stage. The range is 1:1.22 to 1:2.11, averaging 1:1.36 (Table 9).

10. *At 140-150 hour stage:* The effect is still easily seen but weak and transient. The range is from 1:1.12 to 1:1.46, the average being 1:1.28 (Table 10).

B—The effect of adrenaline on heart strips at different stages of development.

1. *3-day stage:*

Sinus preparations: After the addition of the adrenaline generally within a minute the increase of the heart rate is noted. The reaction persists about four minutes, after which the rate returns gradually to normal. The range is from 1:1.11 to 1:1.72, averaging 1:1.30 (Table 11).

Ventricle and apex strips: An increase in frequency and height of contraction is observed. The effect is only transitory, the original condition being regained in 5 to 9 minutes. The range is from 1:1.67 to 1:3.75, averaging 1:2.56 (Table 12).

2. *4-day stage:*

Sinus preparations: Increase in frequency and height is again noted, the range being from 1:1.2 to 1:2.49, averaging 1:1.33 (Table 13).

Ventricle and apex strips: The effect is like that in the 3-day stage except weaker, the range being 1:1.10 to 1:2.70, averaging 1:1.56 (Table 14).

3. *5-day stage:*

Sinus preparations: The reaction is transitory, both frequency and contraction being affected. The range is from 1:1.37 to 1:2.10, averaging 1:1.61 (Table 15).

Ventricle preparations: After two to three minutes a transient decrease of frequency occurs. The rate then gradually returns to normal. The range is from 1:0.32 to 1:0.17, averaging 1:0.46 (Table 16).

4. *6-day stage:*

Sinus preparations: A transient increase in frequency and contraction occurs, ranging from 1:1.25 to 1:1.75, averaging 1:1.45 (Table 17).

Ventricle preparations: The reaction is an initial decrease in frequency which gradually disappears. The range is from 1:0.34 to 1:0.78, averaging 1:0.53 (Table 18).

Apex preparations: Only decrease in frequency is seen; this gradually vanishes. The range is from 1:0.28 to 1:0.70, averaging 1:0.44 (Table 19).

5. *7-day stage:*

Sinus preparations: An increase in frequency and strength of contraction occurs ranging from 1:1.12 to 1:1.66, averaging 1:1.22 (Table 20).

Ventricle preparations: The decrease in frequency is notably more marked, ranging from 1:0.42 to 1:0.86 and averaging 1:0.61 (Table 21).

Apex preparations: The effect is similar to that in younger preparations, ranging from 1:0.24 to 1:0.89, averaging 1:0.57 (Table 22).

DISCUSSION

The results of these experiments show that the automoticity of the heart of the chick embryo is evident as early as the 28th hour, but on the average the period is from 33 to 35 hours after the beginning of incubation. This period synchronizes with the appearance of the 9th somite, as Oliviero Olivo has noted. Ordinarily, if one disects out a heart that has already begun automatic beating and transfers it to warm oxygenated Ringer's solution it continues to beat. The action of adrenaline on the entire extirpated heart is always an increase in frequency regardless of the stage of development.

According to Fujii, the heart does not give any particular reaction to adrenalin in concentration of 0.00002 to 0.001 per cent much earlier than 48 hours after the beginning of incubation, and even on the 4th day of incubation it reacts either lightly or not at all. At the end of the 4th day the stimulating effect of adrenaline is established.

According to our observations throughout the period of 29 to 180 hours of incubation, the heart reacts to adrenaline in concentration of 0.000039 per cent. The reaction is a clean cut increase of frequency and strength of contraction. An explanation of the discrepancy cannot now be offered.

The effect of adrenaline on the heart rate is weakest between the 61st and 70th hours of incubation and strongest between the 91st and 100th hours. According to Oliviero Olivo, at the time heart movements begin nerve fibriles in the heart cannot be seen, hence the heart beat is purely myogenic. His was able to demonstrate the presence of ganglion cells first on the 6th day of incubation. We have frequently confirmed this.

These observations raise the question how the effect of adrenaline on the embryonic chick heart is brought about. According to Kuré adrenaline acts not only on the myoneural junctions but on the heart muscle itself. Morishima likewise demonstrated the direct action of adrenaline on the heart muscle by sectioning the sympathetic inflow and allowing the terminals to degenerate. From these facts we reach the conclusion that adrenaline exerts a direct effect on the heart muscle. Otherwise, we must assume that there are nerve-like structures in the embryonal cells which give this reaction, although in a less pronounced way.

By the investigations with strip preparations it is shown that the tissue at the mouths of the great veins without exception show an increase in frequency and strength of contraction. Such variations as appear are only in the degree of reaction. The greatest frequency is noted at about the 120th hour of incubation. These findings are by no means surprising, for the effect of adrenaline on the heart and on the sinus derivatives at the mouths of the great veins must necessarily be the same.

Interesting are the somewhat less striking results with preparations from the ventricle or apex of the heart. These preparations show, up to the third day of incubation, a strong increase in frequency. The reaction is then reversed as age increases and at the fifth day the frequency, after the application of adrenaline, falls below the normal.

These results coincide with those of Funada. Using preparations of the post-embryonic heart, he found also that adrenaline caused an increase in the contraction and a decrease in the frequency. He noted only a weak effect on auricle strips. We, on the contrary, got a clear cut effect with strip preparation from the region of the mouths of the great veins, which tissue is comparable with that of the auricle.

CONCLUSIONS

1. Experiments with chick embryos have shown that adrenaline causes an increase in the frequency and contraction of heart preparations without regard to stage of development.

2. Amount of acceleration varies with the stage of development, being weakest at the 61st to 70th hours of incubation and strongest at the 91st to 100th hours.

3. The effect is always transitory.

4. Heart strip preparations from the apex region react to adrenaline by decrease of frequency and height of contraction.

5. The course of the reaction corresponds to that of heart preparations in general.

6. Ventricular strip preparations are also stimulated by adrenaline. From the 5th to 7th day of incubation, however, a decrease in the frequency and an increase in the contractions is to be observed.

7. With apex preparations a decreased frequency but an increased contraction occurs.

8. The effect of adrenaline on the strip preparations is transitory, lasting at most only a few minutes.

9. By and large, the effect of adrenaline on the embryonic heart is the same as that on the post-embryonic with the single exception that preparations from the mouths of the great veins show only increased activity.

10. Certain suggestions are made as to the point of attack of adrenaline.

BIBLIOGRAPHY

Fujii: Nippon Yakubutsu Gakkai Zasshi, **4**: 209. 1926.

Aristoteles, Harvey, Aldrovandus, Haller, Prévost und Dumas, v. Baer, Carpenter, Wernicke, Laborde und Laveran: Cited by Tigerstedt, Physiologie des Kreislaufes. Berlin, 1921.

Preyer: Spezielle Physiologie des Embryo. Leipzig, 1885. Pp. 33.

Ohara: Fukuoka Ikadaigaku Zasshi, **16**: 1761. 1923.

Oliviero Olivo: Ber. ü. d. ges. Physiol. u. exper. Pharmakol. **34**: 718. 1926.

Kuliabko: Arch. f. d. ges. Physiol. **90**: 461. 1902. **97**: 539. 1903.

Fano: Zentralbl. f. Physiol. **3**: 325. 1890.

Kuliabko: Zentralbl. f. Physiol. **15**: 588. 1902.

Clark: J. Physiol. **54**: 275. 1920.

His: Abh. d. math. Phys. Kl. d. sächs. Ges. d. Wiss. **18**: 31. 1891.

Kuré: Diagnostik u. Therapeutik d. Herzkrankheiten. Tokio, 1918.

Morishima: Pharmakologie. Tokio, 1927.

Funada: Kyoto Igakkai Zasshi, **23**: 144. 1926.

TABLE I

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
37	88	96	96	88	...	...	...	...	...	...	...
37	72	114	120	120	100	...	...	...	...	...	...
38	56	100	100	108	100	92	...	...	...	...	...
31, 5	88	96	128	136	128	120	100	92	...	...	...
32	60	80	80	60	...	...	...	...	...	...	...
32	112	144	144	120	112	...	...	...	...	...	...
30	104	152	152	132	128	120	104	...	...	...	...
30, 5	62	88	116	100	...	80	72	62	...	...	...
29	40	48	52	48	40	...	...	...	...	...	...
35	64	64	84	84	80	80	...	...	...	...	...
36	48	56	56	68	56	56	48	...	...	...	...
38	88	92	92	100	92	92	...	88	...	...	...

TABLE II

47	70	136	132	120	112	100	88	72	...	...	...
47	62	80	90	86	82	80	72	66	...	...	...
48	46	72	72	68	62	...	54	...	50	...	...
44	66	106	110	102	100	88	76	72	...	...	...
45	74	88	92	104	100	96	88	76	...	...	...
47	62	88	90	84	80	80	76	72	68	...	...
45	100	120	120	148	136	128	116	108	100	...	...
45	104	108	112	112	...	108	...	...	...	...	...
42	108	112	112	120	...	112	108	...	...	...	...
43	120	136	128	128	120	120	...	...	...	...	...
46	76	84	88	88	84	80	76	...	...	...	...
50	56	84	84	72	64	60	56	...	...	...	...

TABLE III

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
54	76	82	120	120	108	100	92	80	76	...	...
56	88	92	144	136	132	120	112	100	92	...	...
52	128	148	160	156	152	144	132	128	...	...	...
51	144	144	148	160	156	144	...	...	...	...	...
53	88	104	112	128	128	112	108	100	92	...	...
52	80	128	128	120	116	108	108	92	88	...	...
57	100	144	144	144	152	160	152	140	128	...	...

TABLE IV

70	148	156	160	160	156	156	152	148	...	...	...
70	144	152	152	148	148	148	144	...	...	...	...
66	122	...	150	150	146	142	136	128	128	...	...
68	130	144	144	147	...	144	136	132	...	...	...
69, 5	76	80	90	90	88	84	80	76	...	...	...
67	128	168	180	180	180	172	...	...	...	...	...
68	140	160	160	180	192	192	192	192	180	...	...
68, 5	140	160	176	176	168	160	...	...	148	...	...
65	140	140	160	160	148	148	140	...	...	...	...
69	140	160	168	168	168	152	...	...	140	...	...
69	140	172	172	168	160	156	...	...	152	...	...

TABLE V

72	104	140	152	156	156	140	132	...	...	...	...
72	66	72	86	86	84	82	78	...	...	...	...
73	85	100	105	...	...	100	88	...	...	...	...
75	152	160	168	160	160	156	152	...	...	...	...
76	144	160	160	160	160	156	152	...	...	...	...
74	108	160	160	140	124	124	124	...	...	...	...
76, 5	120	120	152	160	156	148	148	...	...	...	...
76, 5	156	164	176	168	168	168	160	...	...	...	...
77	96	100	108	124	112	104	100	...	...	...	...
79	100	100	100	148	148	132	124	...	...	...	...
80	120	128	128	140	132	132	...	120	...	...	...

TABLE VI

85	120	140	164	176	168	140	...	...	...	...	...
87	120	140	160	164	140	132	...	...	...	...	...
84	120	156	172	168	156	136	120	...	...	...	...
85, 5	120	168	172	144	136	128	120	...	...	...	...
86	128	168	168	180	180	180	172	164	...	...	...
84	100	136	168	168	168	140	132	120	...	...	...
88	120	132	152	164	156	148	136	124	...	...	...
89	120	128	168	160	152	144	128	120	...	...	...

TABLE VII

93	76	152	128	104	96	88	84	...	...	...	...
94	80	116	88	...	...	...	...	...	...	...	...
95	144	128	128	100	100	96	96	88	...	...	...
96	156	156	156	176	176	160	152	140	...	...	...
96	120	132	132	156	152	140	132	120	...	...	...
98	64	144	80	64	...	...	...	...	...	...	...
98	92	96	104	...	...	...	...	...	...	...	...
99	96	112	108	96	...	...	...	...	...	...	...
100	60	60	68	80	96	80	80	72	...	...	...
100	68	72	80	88	88	76	72	72	68	...	...
100	92	120	144	100	100	100	96	92	...	...	...
92	80	160	176	156	140	132	128	120	100	...	...

TABLE VIII

101	120	172	172	124	120	...	...	...	...	...	...
105	96	148	140	120	116	108	100	...	...	...	...
107	128	128	152	156	156	144	128	...	...	...	...
109	80	80	80	124	128	132	132	120	112	...	...

TABLE IX

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
116	80	92	98	...	...	...	...	...	...	...	...
123	80	100	100	96	80	...	...	...	...	...	...
120	140	160	168	172	168	160	144	...	...	...	...
120	107	144	140	120	120	...	...	...	...	...	...
124	100	112	124	100	...	...	...	...	...	...	...
125	72	128	152	72	...	...	...	...	...	...	...
126	100	128	140	128	100	...	...	...	...	...	...
128	92	108	108	92	...	...	...	...	...	...	...

TABLE X

149	84	100	100	88	84	...	...	...	...	...	...
143	52	76	64	...	...	...	...	...	...	...	...
145	60	84	84	72	60	...	...	...	...	...	...
148	80	100	100	84	80	...	...	...	...	...	...
150	64	80	68	...	...	...	...	...	...	...	...
142	64	72	64	...	...	...	...	...	...	...	...

TABLE XI

54	140	140	160	148	140	...	...	...	...	...	...
54	144	152	160	148	148	144	...	...	...	...	...
52	108	108	108	144	128	128	120	108	...	...	...
53	124	148	164	144	140	128	124	...	...	...	...
53	124	140	160	144	132	124	...	...	...	...	...
52	120	120	136	140	140	152	140	120	...	...	...
53	136	140	156	148	148	140	136	...	...	...	...
54	80	80	80	84	80	80	...	...	...	...	...
49	96	124	124	116	96	...	...	...	...	...	...
48	124	124	160	140	132	124	...	...	...	...	...
47	80	152	156	88	80	...	...	...	...	...	...
46	88	148	136	116	112	88	...	...	...	...	...
46	72	72	84	116	112	104	100	88	72	...	...
50	116	116	120	120	120	116	116	...	...	...	...
51	100	100	136	120	120	116	112	104	104	100	...
52	92	92	128	116	112	112	100	100	96	92	...
54	96	100	104	132	120	116	100	96	...	...	...

TABLE XII

52	72	120	120	100	88	72	...	...	...	...	...
54	56	120	128	112	92	80	68	60	56	...	...
49	44	80	108	68	56	48	44	...	...	...	...
51	32	32	112	88	76	68	64	56	44	...	...
52	52	76	92	92	88	76	64	52	...	...	...
54	32	80	120	108	68	52	40	36	32	...	...
53	38	100	84	64	64	60	40	...	...	...	...
53	48	48	48	92	88	80	60	48	...	...	...

TABLE XIII

76	108	108	120	128	128	124	...	...	...	...	...
76	128	140	148	160	160	148	144	140	...	...	...
76	128	144	152	152	152	148	140	132	128	...	...
79	124	148	144	140	140	132	124	...	...	...	...
77	136	152	152	152	148	140	136	...	...	...	...
77	132	136	140	148	144	140	...	...	...	...	...
78	92	92	92	128	120	100	100	100	92	...	...
78	148	148	148	160	160	152	...	...	...	...	...
78	104	160	156	140	140	132	116	108	104	...	...
76	68	80	84	156	136	128	...	...	...	...	...
76	100	168	160	132	128	120	108	108	100	...	...
77	144	160	168	168	152	144	...	...	...	...	...
77	88	168	136	128	120	112	108	100	...	...	...
77	120	124	124	156	124	120	...	...	...	...	...
75	140	160	160	140	...	...	...	...	...	...	...
75	128	148	180	140	132	132	128	...	...	...	...
76	128	152	176	160	152	148	140	132	128	...	...
74	132	140	152	144	140	...	138	132	...	...	...
74	100	124	168	120	112	108	100	...	...	...	...
74	128	140	160	128	...	...	...	...	...	...	...

TABLE XIV

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
76	40	40	108	96	96	84	76	72	...	...	...
76	60	80	84	72	64	60	60	...	...	...	...
74	60	68	72	60	60	...	...	...	...	...	...
76	48	48	48	60	56	48	48	...	...	...	...
79	40	40	44	40	40	...	...	...	...	...	...
77	72	80	84	72	...	...	...	...	...	...	...
77	56	64	76	56	...	...	...	...	...	...	...
78	48	85	60	48	48	...	...	...	...	...	...
78	48	60	72	56	56	56	52	52	52	48	...
78	60	120	72	...	...	...	...	...	...	...	...
76	40	100	76	60	52	48	40	...	...	...	...
74	52	52	84	64	60	58	52	...	...	...	...
77	52	56	104	52	...	...	...	...	...	...	...
75	100	104	112	108	108	100	...	...	...	...	...
75	108	140	108	...	...	...	...	...	...	...	...
76	68	80	80	92	88	84	72	68	...	...	...
74	108	116	160	156	148	148	132	120	108	...	...
74	64	68	84	64	...	...	...	...	...	...	...
73	92	96	160	148	132	128	120	108	92	...	...
73	80	132	132	136	136	136	136	120	104	94	...
74	108	124	128	140	120	120	120	108	...	...	...
74	68	68	88	68	...	...	...	...	...	...	...

TABLE XV

100	120	180	160	120	...	...	...	...	...	...	...
100	80	92	92	100	88	88	88	80	...	...	...
102	80	140	136	120	100	96	88	88	80	...	...
102	72	144	132	108	108	108	100	92	80	76	...
96	64	136	136	108	108	...	...	...	...	...	...
96	128	176	152	128	...	...	...	...	...	...	...
102	108	140	176	180	180	180	176	172	172	...	...
102	100	140	168	160	156	152	140	...	...	...	...
102	124	152	180	160	152	148	140	132	124	...	...
100	120	120	148	140	132	132	128	120	...	...	...
100	112	144	156	148	140	132	120	...	...	...	...
102	108	140	144	160	152	140	132	128	120	...	...

TABLE XVI

100	64	64	62	24	32	40	...	...	...	...	...
100	64	64	64	48	32	48	...	...	...	...	...
102	48	48	20	20	24	24	28	32	32	...	...
102	68	68	60	52	48	48	52	60	64	68	...
102	76	72	60	24	32	44	60	72	76	...	...
96	80	80	48	52	60	68	72	76	76	80	...
97	72	72	60	32	32	44	68	72	...	...	...
98	76	72	52	36	48	60	72	72	76	...	...
99	60	60	52	32	32	44	56	56	60	...	...

TABLE XVII

120	56	84	72	56	...	...	...	...	...	...	...
122	60	60	100	96	96	84	84	80	76	72	64
122	80	80	116	92	80	...	...	...	...	...	...
123	80	92	100	...	...	...	...	...	...	...	...
125	92	92	152	92	...	...	...	...	...	...	...
124	80	100	100	80	...	...	...	...	...	...	...
124	100	132	104	...	...	...	...	...	...	...	...
124	80	140	104	80	...	...	...	...	...	...	...
124	68	100	84	...	...	...	...	...	...	...	...
124	72	80	128	116	96	88	80	72	...	...	...
125	116	128	140	160	152	148	140	132	...	...	...
125	128	156	164	136	132	128	...	...	...	...	...
125	112	160	144	136	132	120	116	112	...	...	...
125	72	88	88	96	72	...	...	...	...	...	...
125	64	64	64	68	64	...	...	...	...	...	...
124	100	128	124	...	...	...	...	...	...	...	...
124	80	100	108	...	...	...	...	...	...	...	...

TABLE XVIII

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
125	60	60	56	36	40	48	48	60	...	...	...
124	84	60	60	36	32	32	36	40	56	72	...
125	88	88	88	72	76	80	...	...	...	...	...
125	52	52	40	36	44	52	...	...	...	...	...
124	92	92	92	68	72	80	92	...	...	...	...
124	116	104	104	40	48	48	48	56	72	...	...
125	80	80	52	36	40	48	52	60	72	...	...
125	76	76	64	44	52	60	68	72	76	...	...
125	64	64	40	32	36	40	48	56	64	...	...

TABLE XIX

122	60	60	36	28	28	36	48	52	60	...	...
123	80	80	48	44	44	36	37	36	40	56	68
123	76	56	48	48	48	48	44	48	52	60	64
124	64	48	20	24	24	24	28	36	48	52	60
125	52	44	28	24	24	24	28	32	40	52	...
125	68	68	68	32	32	32	28	32	36	44	56
124	68	68	68	52	48	60	72	76	...	...	...
124	76	76	74	40	40	40	48	52	60	68	...
124	76	76	76	36	28	36	40	48	56	60	...
124	64	64	64	28	40	48	52	60	68	72	...
124	76	56	32	40	40	36	36	36	40	48	...
125	88	84	64	40	40	48	56	...	...	...	...
125	56	56	20	36	24	28	36	40	48	56	...
125	80	80	80	20	52	56	64	68	72	76	...
124	76	76	68	44	44	48	52	56	64	68	...
124	68	56	24	44	52	56	56	64	68	...	...
124	68	68	60	48	44	52	64	...	...	...	...
124	64	64	60	44	...	...	...	...	...	...	...

TABLE XX

148	140	144	160	160	156	148	140	...	...	...	...
148	72	76	84	112	112	108	100	...	...	...	...
148	108	112	132	108	...	...	...	...	...	...	...
150	132	140	144	136	136	132	...	...	...	...	...
150	100	100	116	100	...	...	...	...	...	...	...
146	120	140	140	160	148	140	...	...	...	...	...
146	132	148	140	...	...	...	...	...	...	...	...
150	128	140	160	160	144	140	132	128	...	...	...
150	132	140	152	144	140	138	132	...	...	...	...
140	120	120	138	160	152	144	132	128	120	...	...
140	124	140	160	164	152	144	136	124	...	...	...
142	132	148	152	132	...	...	...	...	...	...	...

TABLE XXI

148	88	88	72	52	52	52	56	50	68	72	...
148	64	64	64	36	32	32	36	44	48	56	60
150	92	92	92	64	72	80	84	88	92	...	...
146	80	80	80	60	64	72	76	80	...	...	...
146	88	84	80	60	72	76	88	...	...	...	...
146	84	84	56	64	68	76	80	84	...	...	...
146	76	68	60	32	36	36	72	72	76	...	...
148	60	60	60	52	60	60	...	...	...	...	...
148	92	76	68	60	64	72	76	80	88	92	...
150	96	96	72	48	52	60	68	76	88	96	...
140	76	72	68	36	40	52	60	76	...	...	...
140	80	80	76	52	52	60	68	76	80	...	...

TABLE XXII

Incubation Time, Hours	Initial Rate	After 30 Sec.	After 1 Min.	After 3 Min.	After 4 Min.	After 5 Min.	After 6 Min.	After 7 Min.	After 8 Min.	After 9 Min.	After 10 Min.
148	100	100	96	48	44	40	48	56	64	72	76
148	56	56	56	52	24	32	40	44	48	52	56
148	44	40	37	36	32	28	32	36	40	44	...
148	68	60	56	48	36	40	44	48	56	68	...
150	68	68	52	60	68	...	...	...	...	...	...
150	84	84	42	28	28	36	40	48	56	60	68
150	100	100	88	64	72	84	84	92	100	...	...
150	92	88	60	44	48	48	52	60	64	72	72
146	80	76	72	64	68	68	72	76	80	...	...
146	76	76	76	72	72	72	76	...	...	...	...
146	64	60	52	48	52	60	64	...	...	...	...
148	68	68	44	40	40	44	52	60	68	80	...
150	80	80	64	56	56	60	60	64	72	...	...
150	84	72	48	44	48	56	60	68	72	...	...
150	56	56	32	28	28	36	44	48	56	...	...

THE INFLUENCE OF SUPRARENAL SUBSTANCE ON MUSCLE AUTOLYSIS IN VITRO

T. P. SUN
The Research Institute of the Lankenau Hospital
PHILADELPHIA

INTRODUCTION

From the metabolic point of view the data with respect to the suprarenal gland indicate that it is concerned in the catabolic rather than the anabolic phase. This holds for both cortex and medulla. The rôle of medullary activity in carbohydrate mobilization is too well known to need direct citation. The evidence from the cortical side is indirect but significant. Jaffé (1924) observed that thymus involution was retarded by suprarenalectomy, and that thymus regeneration in older animals occurred under like conditions. Hammett (1928) reported acceleration of thymus autolysis *in vitro* when cortical substance was added to the digest.

As far as tissue autolysis is concerned, but little consistency is found in the literature. Izar and Fagiuolo (1916) reported that suprarenal extract had no effect on liver pulp. Kawashima (1910) found no enzymes in extracts of horse suprarenal cortex. Obie (1923) obtained negative results when muscle was digested with epinephrine or suprarenal extract. Yasusade (1926) saw no influence of epinephrine on phosphoric acid liberations on autolysis of muscle or liver tissue. On the other hand Gruber (1924) and Hoskins and Durant (1923) consider epinephrine acts as a metabolic catalyst.

In view of these reports and the results of Hammett (1928) it seemed desirable to determine the influence, if any, of suprarenal cortex and medulla on muscle tissue autolysis *in vitro*.

In the work described here fresh cortical or fresh medullary tissue was added to fresh muscle tissue of the same animal. The procedure was as follows.

PROCEDURE.

Guinea pigs were killed with ether. Muscle tissue was removed and pulped in a meat grinder. Twelve approximately equal amounts (2 to 3 gms.) of the thoroughly mixed mass were transferred to an equal number of weighing bottles and weighed. Of these 6 were used for controls and 6 for tests. The weighed tissue was moistened with toluene, then ground with fine sand. It was at this point that the bits of cortex or medulla was incorporated into 6 of the muscle tissue samples. While one lot was being ground the others were kept cool in an ice bath. The ground up mass was transferred to a centrifuge tube. To it was added 16 cc. of saline buffered to pH 5.9 with phosphate mixture, and 3 drops of toluene. After thorough

mixing 3 samples containing cortex or medulla, and 3 samples without this addition were incubated at 37° C. for 24 hours. The remaining 6 lots (3 with and 3 without glandular substance) were immediately centrifuged for 10 minutes. To each was added 4 cc. 10 per cent tri-chlor-acetic acid and the mixture again centrifuged. The clear supernatant liquid was then analyzed for NH_2-N according to the method of Van Slyke (1912). The incubated samples were similarly treated.

There was thus had for comparison the NH_2-N, in triplicate, of muscle tissue with and without suprarenal cortex or medulla, before and after incubation.

The phosphorous in the extract was determined according to Fiske and Subbarow (1925). This was done on separate material but treated exactly as described up to the point of precipitation. Here 20 cc. of 10 per cent tri-chlor-acetic acid was added to 5 cc. of the muscle extract and filtered. Ten cc. of the filtrate was used for analysis.

RESULTS

In table 1 are given the figures for initial and terminal NH_2-N values, the percentage increase on incubation, and the difference of the increase of

TABLE I

THE AUTOLYTIC PRODUCTION OF NH_2-N IN MUSCLE TISSUE UNDER THE INFLUENCE OF SUPRARENAL CORTEX AND MEDULLA.

	NH_2-N per cent per gram tissue				Percentage Increase		
	Initial		Terminal				
Expt.	Contl.	Test	Contl.	Test	Contl.	Test	T-C
			CORTEX				
1.	0.0472	0.0386	0.1097	0.0931	132.4	141.2	8.8
2.	0.0596	0.0502	0.1186	0.1120	99.0	123.1	24.1
3.	0.0640	0.0657	0.1267	0.1259	98.0	91.6	–6.4
4.	0.0573	0.0548	0.1000	0.1141	74.5	108.2	33.7
5.	0.0601	0.0624	0.1038	0.1110	72.7	77.9	5.2
6.	0.0534	0.0554	0.1252	0.1267	134.5	128.7	–5.8
7.	0.0591	0.0613	0.1207	0.1258	104.2	105.2	1.0
8.	0.0619	0.0607	0.1162	0.1187	87.7	95.6	7.9
			MEDULLA				
1.	0.0574	0.0584	0.0853	0.0865	48.6	48.1	–0.5
2.	0.0512	0.0550	0.0855	0.0981	67.0	78.4	11.4
3.	0.0534	0.0456	0.0714	0.0842	33.7	84.7	51.0
4.	0.0600	0.0481	0.0694	0.0995	15.7	106.9	91.2
5.	0.0430	0.0438	0.1025	0.1128	138.4	157.5	19.1
6.	0.0480	0.0517	0.0766	0.1002	59.6	93.8	34.2
7.	0.0409	0.0397	0.0859	0.0956	110.0	140.8	30.8
8.	0.0492	0.0458	0.0816	0.0754	65.9	64.6	–1.3

the tests from the controls for both cortex and medulla. In table 2 the like values for phosphorus are given. It is to be noted that the value for each experiment represents the average of determinations on 3 separate samples of muscle tissue; not determinations on 3 aliquots of extract from a single weighed muscle specimen.

The results show that autolysis of muscle tissue proteins giving rise to amino-acids is increased on the average by 8.6 per cent when cortical substance is present and by 29.5 per cent when medullary tissue is added. Since the amount of added gland material was too small to give the increase by itself, the conclusion is that suprarenal accelerates muscle protein autolysis *in vitro*. Whether or not the result with cortex is attributable to possible contamination with medulla is undeterminable from these experiments. The only significant thing that can be said with security is that the evidence is consistent with the idea that the suprarenal may be a participant in the catabolic phase of nitrogen metabolism.

The source of the inorganic phosphorous increase in studies of this nature is indeterminate. There is a possibility that a large part comes from the hydrolysis of phospho-creatine. Apparently medulla has no influence upon this process. It is possible that cortex has an inhibitory effect as reflected in table 2. Unfortunately it was necessary for me to drop this

TABLE II

THE AUTOLYTIC PRODUCTION OF INORGANIC PHOSPHORUS IN MUSCLE TISSUE UNDER THE INFLUENCE OF SUPRARENAL CORTEX AND MEDULLA.

	P per cent per gram tissue				Percentage Increase		
	Initial		Terminal				
Expt.	Contl.	Test	Contl.	Test	Contl.	Test	C-T
			CORTEX				
1.	0.147	0.167	0.197	0.196	34.0	17.4	16.6
2.	0.164	0.188	0.223	0.228	36.0	21.3	14.7
3.	0.175	0.171	0.206	0.196	17.7	14.6	3.1
4.	0.168	0.174	0.199	0.209	18.5	20.1	–1.6
			MEDULLA				
1.	0.181	0.193	0.216	0.226	19.3	17.1	2.2
2.	0.176	0.185	0.214	0.225	21.6	21.6	0.0
3.	0.182	0.189	0.223	0.227	22.5	20.1	2.4
4.	0.189	0.193	0.209	0.213	10.6	10.4	0.2

phase of the work before the point could be established. The figures are merely presented in order that they be on record.

SUMMARY AND CONCLUSION

Autolysis of muscle tissue of the guinea pig was studied with regard to the influence of suprarenal substance thereon. It was found that both cortex and medulla accelerate amino-acid production on incubation, the latter more strongly. Similar studies of inorganic phosphorus liberation gave no sure results. The conclusion is that a metabolic rôle of the suprarenal is that of a participant in catabolism.

BIBLIOGRAPHY

1. Fiske, C. H. and T. Subbarow: The colorimetric determination of phosphorous. J. Biol. Chem. **66**: 375. 1925.
2. Gruber, C. M.: Fatigue. XIV. The effect of adrenalin on the duration of the latent, the contraction, and the relaxation periods of skeletal muscles at rest and undergoing fatigue. J. Pharmacol. and Exper. Therap. **23**: 335. 1924.

3. Hammett, F. S.: Die Physiologie der Thymus. Fortschr. d. Naturwiss. Forschung. N. F. **4**: 1. 1928.
4. Hoskins, R. G. and E. P. Durant: The effect of fatigued muscle upon perfused adrenalin. Am. J. Physiol. **66**: 176. 1923.
5. Izar, G. and A. Fagiuolo: Autolysis and internal secretion. Sperimentale, Arch. di biol. **70**: 265. 1916.
6. Jaffé, H. L.: The influence of the suprarenal gland on the thymus. I, II, III. J. Exper. Med. **40**: 325; 619; 753. 1924.
7. Kawashima, K.: Zur Kenntniss der Rindensubstanz der Nebenninen. Biochem. Ztschr. **28**: 332. 1910.
8. Obie, A.: Action de l'adrenaline et de l'extrait surrenal sur l'excitabilité musculaire. Compt. rend. Soc. de biol. **88**: 585. 1923.
9. Van Slyke, D. D.: The quantitative determination of aliphatic amino groups. II. J. Biol. Chem. **12**: 275. 1912.
10. Yasusada, O.: Uber der Einfluss von Chinin sowie einigen Hormonpräparaten auf den Phosphorsäurespaltung bei Autolyse der Muskultur und der Leber. J. Biochem. (Japan) **6**: 179. 1926.

AN ENDOCRINE CONSIDERATION OF RECKLINGHAUSEN'S DISEASE: REPORT OF A CASE WITH ASSOCIATED CHILDHOOD MYXEDEMA

MURRAY B. GORDON, M.D.

From the Endocrine Clinic, Department of Pediatrics, Long Island College Hospital

BROOKLYN, N. Y.

The simultaneous occurrence of Recklinghausen's disease and endocrine dyscrasia in the same individual has resulted in a discussion of the relationship between the two conditions. Those who have reviewed the literature have arrived at contradictory conclusions. Tucker (1) claims that there is a definite relationship between Recklinghausen's disease and certain endocrine disorders. Levin (2) states that the condition of generalized neurofibromatosis is a clinical entity depending essentially for its etiology upon endocrine dysfunction. Mosbacher (3) infers that the conception of this symptom must be extended to include the simultaneous occurrence of endocrinopathy and to consider all cases in which this is not evident as exceptions. Szondi and Kenedy (4) and Starck (5), who has recently published an extensive review of the entire subject, conclude that while the coincidental advent of both conditions is more than accidental, they are not basically dependent upon one another but upon a common third genetic factor. This view is also held by Dumbrowsky (6), who does not see any causal relationship between Recklinghausen's disease and incretory disorders, since there are cases in which there is no endocrinopathy present and others in which the endocrine dyscrasia appears later. Prange, in Curschmann's monograph on endocrine disorders (7), considers that the pluriglandular insufficiency is only accessory and not in any way causal.

Pende (8) states that two factors are essential for the production of such dystrophies as Recklinghausen's disease: (1) A constitutional factor represented by an abnormality of the endocrine-sympathetic system which may be hereditary; (2) an accidental factor, such as shock, trauma, toxic poison, infection, etc., which through its effect on the endocrine-sympathetic system acts as a stimulus on the embryonal elements. This theory concurs in principle with that of Ewing (9), who considers that the underlying factor in Recklinghausen's disease is a disturbance between the ectoderm and the tissues it enervates, and that under certain exciting conditions the congenital malformation of the ectoderm may develop manifestations of the disease. The consensus of opinion in the literature on the general etiology of neurofibromatosis, without particular reference to the question of endocrine relationship, seems to be that it is of ontogenetic origin, traceable to a developmental anomaly of either the mesoderm or ectoderm or both.

For purposes of orientation, it may be advantageous at this point to briefly consider the important features of generalized neurofibromatosis or Recklinghausen's disease. The first clinical descriptions were published by Kolliker in 1860 and by Virchow in 1863. Recklinghausen in 1882 (10) traced degenerating nerve fibres in several cases and stated that all of the tumors arose from nerve trunks or filaments. His conclusions have been verified by the studies of subsequent investigators.

The disease may have its onset during childhood, remain quiescent for several years and then become reactivated in adult life, or else may be progressive from its inception. The condition may be familial, as shown by Preiser and Davenport (11), who found an incidence of 43.5 per cent in 115 children whose parents were affected with Recklinghausen's disease. Both Starck (5) and Schiff (12) reported its occurrence in three generations. This familial tendency is also present in the incomplete forms as observed by Thiebierge (13), who cites instances of families in which one member showed tumor formation while another displayed pigmentation only.

The cardinal symptoms of the disease are generalized neurofibromatosis, cutaneous pigmentation and mental and psychic alteration. To these may be added cachexia, osseous changes and endocrine dysfunction.

A discussion of the various types of tumor formation included under the general classification of neurofibromatosis will not be attempted here. Suffice it to say that the tumors may be plexiform neuromas, with or without multiple molluscous tumors of the skin, neurofibromata of the nerve trunk or fibroma molluscum. They vary in size from that of a pin point to a goose egg and may occur in any number up to several hundred. The nerves which may be affected are the motor and sensory, the special cerebral with the possible exception of the optic and olfactory, and at times the sympathetic.

Other sites of predilection are the true skin, the subcutaneous tissues and the muscles. At the onset the tumors are soft, but when fully developed are hard and fibrous and may be felt as firm, shot-like, sessile or pedunculated nodules under the skin. They may be discrete or coalesced; if matted together, they give the impression of a strand of cord whose course is discernible as subcutaneous elevations. They may be tender and painful to the touch.

Cutaneous pigmentation consists of diffuse, irregularly distributed patches or sheets varying in color from a cafe au lait to an intense brown, and in size from a pin point to an area which may extend over one-third of an extremity. Light reddish colored areas, naevi, lentigo and freckles may also be present.

Starck thinks that pigmentation is due to either idiopathic degeneration of the germinal layers or to endocrine dysfunction. On the side of an endocrine basis are found many observers, among them Wegelin (14),

Goodhart (15) and Levin (2), who consider it a sign of adrenal insufficiency, while Th. Kocher feels that it is due to thyroid dyscrasia (16).

Mental impairment is so frequently associated with Recklinghausen's disease that many feel that somatic stigmata of degeneration, imbecility, mental aberration and psychic disturbances are integral parts of the complete picture of the disease. Thiebierge (13), Starck (5), Adrian (17), Knoblauch (18) and Speransky (18) have recorded instances of this association.

Incomplete forms with the absence of one or more of the cardinal symptoms have been observed. Thiebierge (13) was the first to describe a type of this disease which is characterized by pigmentation without tumor formation and which is now considered as an incomplete form. Instances of this type have been reported by Herxheimer and Roth (19), Weber (20), Adrian (17), Littlewood (21) and Wise and Eller (22).

Three additional syndromes are considered by Starck (5) as being incomplete forms of Recklinghausen's disease: (1) Leschke syndrome, characterized by cutaneous pigmentation and endocrine dyscrasia with absence of neurofibromata; (2) Laurence-Biedl syndrome, characterized by endocrine dysfunction with absence of both pigmentation and neurofibromata; (3) Cerebral Tuberous Sclerosis (Tuberosa Gehirnsklerose), characterized by cutaneous pigmentation, cutaneous fibromata and tumors of cerebral cortex.

E. Leschke (23), under the term of dystrophia pigmentosa, described a symptom complex occurring in individuals exhibiting the incomplete type of Recklinghausen's disease in association with an endogenous pluriglandular insufficiency. The clinical picture of Leschke's syndrome consists of arrested growth with physical and mental infantilism and increased cutaneous pigmentation in the form of cafe au lait spots, naevi and freckles. Endocrine dysfunction is expressed in obesity, genital hypoplasia, impaired carbohydrate metabolism, low blood pressure, hypotonia and asthenia. Giantism or signs of hypothyroidism may also be present. Vegetative nervous system changes are evidenced by increased irritability of the sympathetic and parasympathetic systems. Instances of this syndrome have been observed by Leschke (24), Ulmann (24), Hoffmann (25), Galant (26), and Barber and Shaw (27).

Biedl in 1922 (28) described a form of cerebral obesity which had previously been observed and reported by Laurence and Moon in 1866 (29), the predominating symptoms of which are : (1) Dystrophy adiposa genitalis, expressed in obesity and genital hypoplasia; (2) congenital maldevelopment, such as retinitis pigmentosa, atresia ani and polydactylitis; (3) skull deformities, as macrocephalus, microcephalus, tower-skull, and asymmetry; (4) mental delinquency.

Solis-Cohen and Weiss (30) reported four cases in 1925, all of the patients showing a reduction of the basal metabolic rate. Bernhardt (31) observed two patients with this syndrome. Both were of the vagotonic type

with normal metabolic rates. The sella turcica was found normal on radiographic studies in both patients. One of the patients showed symptoms of diabetes insipidus. Zondek (32) reported two cases of this type. A simultaneous hypophyseal dyscrasia was reported by Bohn (33).

Tuberous sclerosis of the brain is a condition which is thought to be due to mal-development of the mid-brain (Starck) and is characterized by tumor-like foci in the cerebral cortex and ventricular walls. Other organs may also be studded with multiple sclerotic nodules. The clinical picture consists of neurological and mental aberration, such as epilepsy, idiocy and signs of mid-brain pressure; cutaneous pigmentation, as freckles, naevi, cafe au lait spots and lentigo; cutaneous fibromata on neck and back.

Orzechowski and Nowicki (34) and Pick and Bielschowsky (35) think that a relationship exists between tuberosa sclerosa and Recklinghausen's disease. Schuster (36) observed families in which tuberosa sclerosa occurred in one member and Recklinghausen's disease in another.

While Starck feels that Recklinghausen's disease, Leschke's syndrome, Laurence-Biedl syndrome and tuberosa sclerosa are all expressions of the same ontogenetic mal-development, the majority of investigators do not mention the Laurence-Biedl syndrome nor tuberous sclerosis in this connection (37).

According to Starck (5) the condition of the affected endocrine glands in Recklinghausen's disease falls into one of three groups: (1) A tumor of either the endocrine gland itself or of the surrounding neighborhood producing pressure symptoms, as in tumors of the hypophysis or mid-brain; (2) functional disturbance without anatomical alteration; (3) functional disturbance with anatomical lesions, such as in anomalies.

The glands which have been reported as having been involved are the thyroid, parathyroid, pituitary, adrenals and gonads.

Thyroid dysfunction was frequently encountered. Cretinism was observed by Adrian (17), Strohmeyer (38), Schuh (39) and Ottolia (40). Schiffner (41) reported the occurrence of association with cretinism in two brothers. Andueza's patient was a cretin presenting a neurofibroma in the region of the thyroid (42). Pic and Rebattu (43) and Meige and Feindel (44) reported myxedematous symptoms in their patients. Hypoplasia and hypothyroidism were observed by Dumbrowsky (7) and Roederer (45). The mother of the latter's patient had cutaneous pigmentation. Ehrmann (46) reported two cases, in one of which the thyroid was small and in the other was entirely absent. Thyroid infantilism, pigmentation and neurofibromatosis were found associated by Debove (47). Galant's patient had a combination of Leschke's syndrome, mongolian idiocy and myxedema (26). Hyperthyroidism and goiter were encountered by Hallopeau and Ribot (48) and Bourcy and Laignel-Lavastine (49). According to Levin (2), the only case of Recklinghausen's disease associated with parathyroid tetany was reported by Schlesinger (50).

A diagnosis of hypophyseal dysfunction was made on the presence of acromegaly, giantism, polydypsia, polyuria, and dystrophia adiposa genitalis. Pituitary involvement was observed by Feindel and Froussard (51), Piollet (52), Nicolas and Favre (53), Cushing (54), Wolfsohn and Marcuse (55), Raymond and Alquier (56), Roubinowitsch and de la Sourdiere (57), Mann (58), Escher (58), Tucker (1), Barker (58) and Bittdorf (58). De Castro (59) reported the association of a pituitary tumor, acromegaly and Recklinghausen's disease. Lier's patient (60) was a boy of 9 years who presented a typical picture of Froelich's syndrome and a generalized neurofibromatosis. A roentgenographic examination revealed a tumor close to the hypophysis. Spillman (61) reported a case of tumor of the sella turcica.

Adrenal insufficiency was frequently noted. According to Levin, at the time of his report (1921), there were approximately 50 instances in the literature with so-called Addisonian symptoms, an incidence which he felt was too low. A diagnosis of adrenal insufficiency was made in most cases on asthenia, low blood pressure, pigmentation and hypotrichosis. The same investigator reviewed 14 autopsy reports in the literature in which the findings in the glands of internal secretion were included and found adrenal disease in 12.

Gonad association is evidenced by onset of symptoms of Recklinghausen's disease at the time of puberty and their aggravation at the time of menstruation, pregnancy and menopause. An illustrative example of this association is Starck's patient, whose symptoms will be considered later. Levin (2) cites several instances of simultaneous occurrence of gonad dysfunction and Recklinghausen's disease.

Pluriglandular involvement is recorded by Tucker (1), Levin (2), Roederer (45), Mosbacher (3), Castronuovo (62) and Starck (5).

Starck had an excellent opportunity of studying his patient for over 23 years. She first came under his observation at a little above two years of age, presenting a combined picture of rickets, scoliosis, cutaneous pigmentation and severe Basedow's disease. The latter was considered by the author to be the result of psychic trauma. The hyperthyroidism was at its height at the age of 4 years, but in the 9th year coincidental myxedema made its appearance. During childhood, the patient was subject to psychic and nervous disturbances in the form of choreiform movements, outbursts of temper, ferocious habits and incompatability in regard to her playmates. Her mentality was always below par.

Pituitary disturbance expressed in diabetes insipidus was first noted at the age of 9 years. At 12 years of age, the left arm began to increase in length and at 21 years the right became affected. This increase in size of the extremities is considered as evidence of acromegaly by Starck, who cites several similar instances in the literature (5).

Menstruation began at 14 years of age and continued regularly until the time of pregnancy at 25 years. Pregnancy was accompanied by an

increased functional activity of the thyroid gland, with an increase in the size of the goiter, which had remained quiescent since the age of 9 years. The symptoms of hyperthyroidism receded after the birth of the child. The cutaneous pigmentation, which had been noted early in the history, and a fibroma molluscum, which had appeared at 22 years of age, increased in size and intensity of color during the period of gestation. Neurofibromatosis was first noted at 17 years of age.

CASE REPORT

J. S., 9½ years of age, is the only child of parents who are not related by consanguinity, and who do not give any history of neurofibromatosis, mental aberration or cutaneous pigmentation on either side. Born at term, he was only three pounds in weight, puny and cyanotic. He was nursed for three months and then placed on artificial feeding. His developmental history shows retardation in both mental and physical fields: teething began at eighteen months of age, walking at two years and talking at three years.

At the time of his initial visit, April 15, 1926, he presented a typical picture of childhood myxedema, with a round moon face, retrousse nose, dry hair, dry skin, cold extremities, high arched palate, pot belly and umbilical hernia. The tonsils were hypertrophied. There was an incurving of the little finger of each hand. Rachitic condition was manifested by flaring of the ribs and enlarged epiphyses. Fluoroscopic examination of the chest revealed a normal thymic shadow. Roentgenographic study of the sella turcica demonstrated a sella of oval contour, type B (Gordon and Bell classification) (63), and within normal limits as to size. The anterior and middle clinoid processes were well seen and the dorsum sellae well developed. No erosions were found. Examination of the fundi of the eyes showed that the nerve was small, slightly pale in color, and vessels of normal size but tortuous. There was a refractive error for which glasses were prescribed. The Wassermann reaction was negative. He was both underweight and underheight (44 pounds and 43 inches).

His speech was indistinct and his mentality below normal for his physical age. He was friendly, with well developed social tendencies, evidenced by desire to play with other children and his amicable attitude toward strangers.

The hypothyroid condition had been recognized at two years of age and he had been under thyroid treatment since then.

He was placed under intensive treatment, resulting in marked improvement in both physical and mental retardation. An intelligence test performed on Aug. 3, 1927, at the Neurological Institute of New York revealed the following:

"The physical age of the patient is 7 years and 4 months but he attains a mental age of 4 years and 10 months with an intelligence quotient of .66 on the Terman scale. This quotient places him among the high grade morons. He was most friendly and co-operative throughout the entire test. His alert and friendly attitude tends to make one feel that he would test higher than he does. He is very observant and asks questions about things in the room. He responds to praise by putting forth more effort.

"At year IV he has a basal age on the test. With the Vth year series, he succeeded in giving definitions superior to use and carrying out three commissions but fails the remaining tests of the level. With the VIth year tests, he has three successes but fails in reconstruction of mutilated pictures, in the comprehension of simple situations and the naming of coins. His upper limit is reached in the VIIth year."

On June 22, 1927, the first signs of neurofibromatosis were noted in the form of numerous cartilagenous-like nodules giving the impression of buckshot under the skin. These were of fairly general distribution, but more pronounced on the back. Discrete cutaneous pigmentation of light brown color was noted over several parts of the body. A pigmented mole was present on the dorsum of the left foot.

Complete examination on Oct. 22, 1929, revealed the following picture: Weight, 54 pounds; height, 47 inches. The face is not as myxedematous as formerly. The teeth are all of the first set, are well placed and in good condition. The tongue is not hypertrophied. Glasses are still worn.

The skin shows a mottled marble like appearance. Numerous pigmented spots are present ranging in size from a pin point to 2 by 1.2 cm. and in color from light cafe au lait to an intense dark brown with some a light reddish tint. Some of the pigmented areas overlie the subcutaneous nodules, but the majority do not.

Plexiform, cartilagenous-like, fibrous nodules which are movable and sessile are felt in the skin, subcutaneous tissue and muscles. These are both discrete and matted together, giving the impression of strands of knotted cords. Elevations under the skin produced by the nodules may be seen through the skin. There are perhaps hundreds of these small nodules covering the entire body.

There is a hypertrichosis especially pronounced on the skin of the back; the hair is not as dry as formerly.

The abdomen is distended, more so during the past few weeks, but no intra-abdominal tumors are discernible.

The external genitalia are of fair size, both testes are undescended and the scrotum shows a ridge in the median line, producing an appearance not unlike that of the labia majora.

Mentally, he has improved to the point where he is beginning to spell words and speak well, but in a rapid fire manner. He reads signs in the street cars and takes an active interest in his surroundings. He has been masturbating for some time.

For the past five years he has been receiving one grain each of the thyroid extract and pituitary substance three times a day on alternate weeks.

COMMENT

The relationship between endocrine disorder and Recklinghausen's disease may be based on one of three possibilities: (1) The endocrine disorder is the fundamental causal factor in the production of the complete picture; (2) the endocrinopathy and the symptomatology of Recklinghausen's disease (generalized neurofibromatosis, cutaneous pigmentation and mental or psychic aberration), while not dependent upon one another, are produced by a common third genetic factor; (3) the simultaneous occurrence of both conditions is accidental without any further significance.

The numerous instances of simultaneous occurrence of both conditions infers an intimate as against an accidental association. Starck's patient, who was under observation for 23 years, affords an opportunity for study of this correlation. At the time of reporting, she presented active signs of both Recklinghausen's disease and of pluriglandular endocrinopathy, the symptoms having appeared in the following chronological order: Pigmentation and hyperthyroidism, myxedema, diabetes insipidus, acromegalic lengthening of the extremities, neurofibromatosis with increase in pigmentation, fibroma molluscum, pregnancy accompanied by an increase in thyroid activity, and in the color and extent of pigmentation and of the fibroma molluscum, and finally birth of a child, to be followed by recession of the hyperthyroidism and increase in size of the fibroma molluscum and in the intensity of the cutaneous pigmentation.

The effects of pregnancy and of other gonad periods on the general endocrine system are too well known to be discussed here. If the cutaneous pigmentation and fibroma molluscum are considered as integral parts of the complete picture of Recklinghausen's disease, then the influence of pregnancy on these two symptoms in this patient were as definite as on the endocrine system. It must be remembered, however, that pigmentation and fibroma molluscum gravidarum may appear during an otherwise normal pregnancy in women who are not suffering from Recklinghausen's disease, and disappear on the culmination of the gestation. Further analysis of

this case shows that while there was a simultaneous change in the general picture of the disease throughout the years, there was evidently no effect noted during pregnancy on the generalized neurofibromatosis.

Conceding that cutaneous pigmentation and cutaneous fibroma are definite and integral parts of the complete symptom complex, and that alterations took place in these two symptoms simultaneously with changes in the endocrine system, it is not definitely proved that the endocrine disorder was at the basis of the entire picture.

This conclusion is also permissible on analyzing the case reports in the literature. Nothing tangible has been advanced to prove conclusively that endocrine dyscrasia is the etiological factor in the causation of this disease. Endocrine association occurs too often perhaps to be merely accidental, but the most that may be assumed is that a third common genetic factor is responsible for both sets of symptoms.

This conclusion, based upon analysis of the clinical pictures described in the literature, is strengthened by the results obtained in this disease by means of organotherapy, even though it may not be justifiable at the present time with our limited knowledge of the endocrines to confirm or rule out endocrinopathy by therapeutic tests. The results obtained with organotherapy are open to interpretation from two viewpoints: the effect on the endocrine dyscrasia and on the disease itself. Unfortunately the scant information to be gleaned from the literature is both conflicting and confusing, due to the failure in some reports to analyze the results from these viewpoints.

This is especially true of instances in which there was an associated Addisonian syndrome of asthenia, low blood pressure, nervousness and gastro-intestinal disturbances in addition to the pigmentation. Amelioration of such symptoms can be considered only as improvement in the adrenal insufficiency and not in the condition of the disease itself. For instance, Revilliod (64) states that he "controlled" symptoms in a patient with an associated Addisonian syndrome to the extent that asthenia disappeared on the administration of adrenal extract and reappeared on its withdrawal. The effect on the tumors is not given. Chauffard and Rodin (65) reported that organotherapy by means of suprarenal extract produced "notable and immediate amelioration" in the signs of suprarenal insufficiency. They also cited cases of Pic and Rebattu (43) and Jullien (66) in which good results were obtained in those symptoms due to suprarenal dyscrasia. Gabriel (67) tried adrenal therapy in two cases of associated osteomalacia and obtained noted improvement in pulse frequency and in the general feeling of well-being, but on the other hand found that the therapy had no remarkable influence on either the osteomalacia or Recklinghausen's disease. Castronuovo (62) instituted adrenin treatment in a patient who had an associated tubercular affection and reported that his patient showed some amelioration of symptoms. This probably consisted of an improvement in

the general condition, as no mention is made of the state of the neurofibromatosis.

The only instance reported in which there was an effect on the fibromatosis was that obtained by Andueza (42). His patient was a cretin who presented neurofibromata in the region of the thyroid, small cutaneous fibromata, cutaneous pigmentation, and signs of thyroid dysfunction. Under ten months of thyroid therapy beneficial results in both endocrine symptoms and in the tumors themselves were noted. The fibroma underwent slow regression in both size and extent, many of them disappearing, and there was an improvement in the endocrine dysfunction.

Adverse results are recorded by Schoonheid (68), who made use of ovarian extract, and Preiser and Davenport (11), who obtained no results with either thyroid or adrenal extract in their patient, who died of progressive asthenia. Curschmann (6) feels that if an associated thyroid insufficiency cannot be improved with thyroid extract, the prognosis does not appear to be hopeful.

In the present case, endocrinopathy was noted early in life, organotherapy was instituted at the age of two years and continued regularly from then on. Signs of neurofibromatosis first appeared at seven years of age, and in spite of intensive treatment the tumor formation has increased in size and extent. Pigmentation, which was not present at the time of his first visit to our clinic, has since appeared with increasing intensity of color and distribution. The endocrinopathies, however, have responded to treatment by an improvement in both mental and physical retardation. An analysis of the results of treatment with thyroid extract extending over a period of seven years demonstrates that this type of treatment had absolutely no effect on either the neurofibromatosis or on the pigmentation, but on the other hand had a beneficial influence on the thyroid dyscrasia.

This would indicate that the existence of the relationship between the two sets of symptoms in this patient was not dependent on the endocrine dyscrasia.

SUMMARY AND CONCLUSIONS

A boy of 9½ years of age presents at the time of reporting a picture of typical childhood myxedema, mental retardation, cutaneous pigmentation and generalized, plexiform, subcutaneous neurofibromatosis. The symptoms of thyroid dysfunction were first noted at the age of two years, at which time he was placed on thyroid treatment. In spite of active organotherapy for the next five years, signs of Recklinghausen's disease appeared at the age of seven years. Intensive thyroid treatment has been continued since then.

The treatment with thyroid extract has resulted in an amelioration of the physical and mental retardation due to the thyroid dyscrasia, but has had no effect on the progress of Recklinghausen's disease. On the contrary, the symptoms of the latter have been aggravated during the past year.

The late appearance of cutaneous pigmentation and generalized neurofibromatosis in spite of intensive organotherapy over a number of years, and their exaggeration in the face of continued intensive treatment, seems to indicate that the symptoms of Recklinghausen's disease in this patient are not dependent upon endocrine conditions.

An analysis of the literature from an endocrine viewpoint forces the conclusion that nothing definite nor tangible has been advanced to prove that endocrine dyscrasia is the etiological factor in the production of generalized neurofibromatosis. While endocrine association occurs too often to be merely accidental, the most that may be assumed is that a third, common genetic factor is responsible for both sets of symptoms.

BIBLIOGRAPHY

1. Tucker, B. D.: von Recklinghausen's disease with special consideration of the endocrine connection. Trans. Am. Neurol. Ass., 1923, p. 34.
2. Levin, O. L.: Recklinghausen's disease: Its relation to the endocrine system. Arch. Dermat. & Syph. **4**: 302. 1921. (With literature up to 1921.)
3. Mosbacher, F. W.: Recklinghausen's disease and pluriglandular disturbances. Arch. f. Psychiat. **88**: 163. 1929.
4. Szondi, L. D. Kenedy and D. Miskolczy: Die Beziehungen des Morbus Recklinghausen zum endokrinen System, Arch. f. Dermat. u. Syph. **148**: 519. 1924-25.
5. Starck, H.: Dystrophia ontogenetica Recklinghausen. Deutsches. Arch. f. klin. Med. **162**: 68. 1928.
6. Curschmann, H.: Endocrine Disorders, Oxford University Press, London, 1929.
7. Dumbrowsky, A.: Ueber die Recklinghausensche Krankheit. Dermat. Wchnschr. **85**: 1513. 1927.
8. Pende, quoted by Levin from Muto: Riv. di pat. nerv. **15**: 656. 1910.
9. Ewing, J.: Neoplastic diseases. W. B. Saunders, Phila. 1919.
10. von Recklinghausen, F.: Ueber die multiplen Fibroma der Haut and ihre Beziehung zu den multiplen Neuromen. Hirschwald, Berlin, 1882.
11. Preiser, S. A. and C. B. Davenport: Multiple neurofibromatosis (von Recklinghausen's disease) and its inheritance. Cold Spring Harbor, 1918.
12. Quoted by Starck (5).
13. Thiebierge, B.: Un cas de maladie de Recklinghausen sans fibromes cutanees ni fibromes nerveux. Bull. et mém. Soc. méd. d. Hôp. de Paris, **15**: 143. 1898.
14. Quoted by Starck (5).
15. Goodhart, S. P.: In Practice of Medicine, by F. Tice; W. F. Prior, Hagerstown, Md. **10**: 665. 1921.
16. Kocher, Th.: Quoted by Starck (5).
17. Adrian, C.: Ueber Neurofibromatose und ihre Komplikationen. Bruns' Beitr. z. klin. Chir. **31**: 1. 1901; also, Multiple Neurfibromatose. Centralbl. Grenzgeb. d Med. u Chir. **6**; 81. 1903. (Contains review of literature up to 1903.)
18. Quoted by Starck (5).
19. Naturforscher Vers. Wien, 1913, p. 184.
20. Weber, F. P.: A note on syndromes sometimes associated with retinitis pigmentosa and pigmentary forms of Recklinghausen's disease. M. Press. **170**: 416. 1925.
21. Littlewood: quoted by Starck (5).
22. Wise, F. and J. J. Eller: Recklinghausen's disease without tumor formation. J. A. M. A. **86**: 86. 1926.
    Eller, J. J.: Neurogenic and psychogenic disorders of the skin. M. J. & Rec. **129**: 481, 554, 616. 1929.
23. Leschke, E.: Berl. med. Gesell. **6**: 21. 1922.
24. Leschke und Ulmann: Pigmentation und endokrine Dystrophie. Zeit. f. klin. Med. **102**: 388. 1926.
25. Hoffmann: Dystrophie Adiposagenitalis, Deutsche med. Wchnschr. **46**: 1266. 1920.
26. Galant, J. S.: Dystrophie pigmentosa und Neurofibromatosis. Med. Klin. **7**: 250. 1927.
27. Barber, H. and M. W. Shaw: Recklinghausen's disease with pituitary tumor. Brit. J. Dermat. **34**: 207. 1922.
28. Biedl, A.: Deutsche med. Wchnschr. **48**: 1630. 1922.
29. Laurence, J. J. and A. C. Moon: Four cases of retinitis pigmentosa occurring in the same family and accompanied by general imperfections of development. Opthal. Review, **2**: 32. 1866.
30. Solis-Cohen, S. and E. Weiss: Dystrophia adiposa genitalis with atypical retinitis pigmentosa and mental deficiency—the Laurence-Biedl syndome. Am. J. M. Sc. **169**: 489. 1925.

31. Bernhardt, H.: Ein Betrag zur Laurence-Biedlschen Krankheit. Ztschr. f. klin. Med. **107**: 488. 1928.
32. Zondek, H.: Die Krankheiten der endokrinen Drusen. 2 ed. Springer, Berlin, 1926; also Ueber plurigiandular insuffizienz. Deutsche. med. Wchnschr. **49**: 339. 1923.
33. Bohn, H.: Ueber ein Fall von Recklinghausenscher Neurofibromatosis mit gleitzeitige Hypophysenerkrankung. Stuttgart. Arzt. Verein, **12**: 7. 1922.
34. Orzechowski and Nowicki: Zur Pathogenese und pathologischen Anatomie der multiplen Neurofibromatose und der Sclerosis tuberosa (Neurofibromatosis universalis). Ztschr. f. d. ges. Neurol. u. Psychiat. **11**: 257. 1912.
35. Pick and Bielschowsky: Uber das System der Neurome und Beobachtungen an einem Ganglienneurom des Gehirns. Ztschr. f. d. ges. Neurol. u. Psychiat. **6**: 391. 1911.
36. Schuster, P.: Beitrage zur klinik der tuberosen Sklerose des Gehirns. 7 Jvers. d. Ges. dtsch. Nervenärzte, 1913.
37. Beck, H. G.: The Laurence-Biedl syndrome. Reports of two cases in one family. Results of treatment. This Journal, **13**: 375. 1929.
38. Strohmeyer: Quoted by Adrian, 1903 (17).
39. Schuh, F.: Quoted by Adrian, 1903 (17).
40. Ottolia, D.: Considerazioni sopra un caso di morbo di Recklinghausen. Riforma méd. **24**: 1243. 1908.
41. Schiffner: Quoted by Levin (2).
42. Andueza, P. H.: Un caso de enfermedad de Recklinghausen con trastoruos endocrinos. Med. ibera, No. 256. 241: 1922.
43. Pic and Rebattu: Un cas de maladie de Recklinghausen. Lyon méd. **108**: 636. 1907.
44. Meige and Feindel: Infanilisme myxoedémateux et maladie de Recklinghausen. Rev. neurol. **11**: 857. 1903.
45. Roederer, J.: Maladie de Recklinghausen avec insuffisance polyglandulaire. Reunion dermat de Strasburg, May 14, 1922.
46. Ehrmann: Zwei Falle von Neurofibromatose. Quoted by Levin (2).
47. Debove: Sur un cas de neuro-fibromatose de Recklinghausen. J. de méd. et de chir prat. **76**: 566. 1905.
48. Hallopeau and Ribot: Un cas de maladie de Recklinghausen avec prédominance des troubles pigmentaires et volumineuse tumeur profonde. Ann. de dermat. et syph. **3**: 613. 1902.
49. Bourcy, P. and Laignel-Lavastine: Un cas de maladie de Recklinghausen. Bull. et mém. Soc. méd. d. Hôp. de Paris, **22**: 21. 1905.
50. Schlesinger, H.: Multiple Neurofibroma der peripheren Nerven und der Nervenwurzeln, mit Beinphänomen. Mitt. d Gesellsch. f. inn. Med. u Kinderh. **10**: 124. 1911.
51. Feindel and Froissard: Dégénerescence et stigmates mentaux, malformation de l'ectoderme, myoclonie épisodique, acromégalie possible. Rev. neurol. **7**: 46. 1899.
52. Piollet, P.: Neuro-fibromatose généralisée. Gaz. d Hôp. **75**: 1345. 1902.
53. Nicolas, J. and M. Favre: Acromégalie et maladie de Recklinghausen. Lyon méd. **114**: 786. 1910.
54. Cushing, H.: The Pituitary Body and its Disorders. J. B. Lippincott Co., Phila. 1912.
55. Wolfsohn, G. and E. Marcuse: Neurofibromatosis und Akromegalie. Berl. klin. Wchnschr. **49**: 1088. 1912.
56. Raymond, F. and L. Alquier: La maladie de Recklinghausen. Ses variétiés nosolgiques. L' Encephale, **3**: 6. 1908.
57. Roubinowitsch and de la Sourdiere. Quoted by Tucker (1).
58. Quoted by Starck (5).
59. de Castro, A.: Sur la coexistance de la maladie de Recklinghausen avec acromégalie. Nouv. iconog. de la Salpêtrière, **25**: 41, 1912.
60. Lier, W.: Ueber Neurofibromatose, Ztschr. f. klin. Med. **80**: 261. 1914.
61. Snillman: Neurofibromatose et tumeurs cérébrale. Gaz. hebd. de méd. **5**: 320. 1900.
62. Castronuovo, G.: Neurofibromatosi diffusa (Morbo di Recklinghausen). Riforma med. **36**: 817. 1920.
63. Gordon, M. B. and A. L. L. Bell: A roentgenographic study of the sella turcica in normal children. This Journal, **7**: 52. 1923.
64. Revilliod, H.: De la neurofibromatose généralisée et de ses rapports avec l'insuffience des capsules surrénales. Thèse, Genève, 1900.
65. Chauffard, A. and P. Brodin: Maladie de Recklinghausen avec syndrome fruste d'insuffisance surrénale. Bull. et mém. Soc. méd. Hôp. de Paris, **44**: 166. 1920.
66. Jullien, A.: Neurofibromatose généralisée. Thèse, Paris, 1910.
67. Gabriel: Fall von Recklinghausenscher Krankheit mit Osteomalacie. Berl. klin. Wchnschr. **48**: 133. 1911.
68. Schoonheid: Nederl. Tijdschr. v Geneesk. **2**: 1639. 1913.

PITUITRIN HYPERGLYCEMIA AND ITS POSSIBLE VALUE IN DIAGNOSIS

PROF. G. MARAÑON AND DR. J. MORROS
Medical Department, Hospital General Madrid,
MADRID

That hypophyseal secretion has some influence on carbohydrate metabolism is well known. This belief is based on the following data, which are well known to modern pathologists:

a. In cases of acromegaly (hyperpituitarism) glycosuria is frequent, with or without symptoms of diabetes. Even when there is no spontaneous glycosuria, hyperglycemia and reduction of the carbohydrate tolerance are frequently noted.

These facts have been confirmed in many clinics. Perhaps the most extensive experiments in this respect are those of Cushing (1), and Davidoff and Cushing (2), whose statistics refer to 100 cases of acromegaly. Yater (3), who studied 79 acromegalic patients, found glycosuria in 10 per cent of them. We have observed 4 glycosuria cases in 26 acromegalic patients (15 per cent), but the figure of 25 per cent given by Bauer (4) seems excessive.

Almost all authors mention spontaneous hyperglycemia in cases of acromegaly, even when there is no glycosuria. We have, however, been unable to confirm this, as is shown by the following table:

TABLE I

BLOOD SUGAR IN 13 CASES OF ACROMEGALY

Case	Diagnosis	Blood Sugar
I	Typical acromegaly	0.77
II	Typical acromegaly and intermittent glycosuria	1.33
III	Typical acromegaly	1.10
IV	Typical acromegaly	0.77
V	Typical acromegaly and intermittent glycosuria	1.38
VI	Typical acromegaly	1.04
VII	Typical acromegaly	0.90
VIII	Typical acromegaly	1.00
IX	Typical acromegaly and ovarin atrophy	0.83
X	Acromegaloid syndrome	0.80
XI	Familial acromegaloid syndrome	1.00
XII	Familial acromegaloid syndrome	1.00
XIII	Juvenile acromegaloid syndrome	0.75

These results can be summarized as follows:

TABLE II

	Hyperglycemia (above 1.2)	Normal Blood Sugar (between 1.2 and 0.8)	Hypoglycemia (below 0.8)
Number of cases	2	8	3
Percentages	15%	61%	23%

This gives a proportion approximately the same as found when blood sugar is studied in any series of patients of any other kind.

b. On the other hand, in hypopituitary syndromes, especially in the genital-adiposity of Frölich, diabetes is very rare, and an increase of the carbohydrate tolerance is almost always observed.

The authors mentioned above, as also many others, have verified this detail sufficiently. As a matter of fact, the tendency towards adiposity of a considerable group of hypopituitary patients has been attributed to this very sluggishness of the carbohydrate metabolism. In my series of 115 hypopituitary patients of all kinds (adiposo-genital syndrome, hypophysial cachexia, hypophysial dwarf growth), I have found spontaneous glycosuria in only two cases: a father and son, both affected with typical adiposity, genital insufficiency and hypophysial tumor. I note that similar cases are mentioned by Shapiro and Kliatshko (5).

c. The injection of the pituitary extract causes hyperglycemia and sometimes glycosuria.

This statement is based on the experience of numerous investigators and clinical observers. Reference is made to the literature mentioned in our book (6). Among recent authors we would mention Hines, Leeese and Boyd (7), La Barre (8), Nitzescu and Benatato (9), Nitzescu and Ramneato (10), Fritz (11), Clark (12), etc.

We shall see later that our experience in the human clinic warrants our stating that this pituitary hyperglycemia is really an almost constant phenomenon, but of slight intensity, except in a few patients; but the principal interest of this hyperglycemia resides precisely in its selectivity.

d. Extirpation of the hypophysis raises the carbodydrate tolerance.

Mention is made in our book (6), which we have already quoted, of the literature dealing with this question. Among recent reports, we would also mention those of the Houssay school (13) and of Pikkat (14), according to whom the hypoglycemia and the resistance to glycosuria is one of the most constant effects of the extirpation of the hypophysis of dogs, after the first few hours during which a transitory glycosuria may appear, and which may be attributed to the narcosis and an incidental lesion of the diencephalic centers. This author differentiates sharply between the humoral hypoglycemic effect, following extirpation of the hypophysis, and the nervous hyperglycemic effect due to the lesion of the neighboring diencephalic centers. For this reason we call attention to his work, as this detail of the glycosuria has created considerable discussion among physiologists as to the glandular or nervous origin of several of the phenomena which follow on the lesion of the hypophysial region.

e. The injection of pituitrin opposes and eliminates the hypoglycemic syndrome produced by insuline.

Ever since the time of Burn's experiments on rabbits (15) and Houssay's on dogs, this antagonistic action of pituitrine on insuline hypoglycemia has been known. In the human clinic, our experience shows that this action is much slower and less certain than that of adrenaline, so that from a practical point of view we should not recommend pituitrine to be resorted to as a treatment for hypoglycemic accidents.

f. The extirpation of the hypophysis increases the organism's sensibility to insuline hypoglycemia.

Houssay and Magenta (16) were the first to prove this. Whilst a dog deprived of the hypophysis is subject to grave hypoglycemic accidents, and even dies after the injection of the usual doses of insuline, a normal dog is subject neither to great decreases in the glycemia nor to important accidents, when treated with the same dose. Olmstead and Logan (17), Geiling, Campbell and Ishikawa have confirmed these experiments (18).

Our experience in the human clinic does not, however, agree with these experimental data, for in three cases of hypophysial lesion with hypofunctional syndrome, the test of the injection of 10 units of insuline was totally negative. We would state here that this same dose of insuline produces appreciable, and sometimes very intense, accidents in subjects whose defensive system against the hypoglycemia has been modified, as, for instance, addisonians, certain hyperthyroid states, hepatic diseases, etc. (19).

TABLE III

SENSIBILITY TO INSULINE IN HYPOPITUITARISM

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 10 Units Insuline			Clinical Phenomena
			30′	60′	120′	
I	Hypophysial tumour (adiposogenital syndrome)..	0.95	0.80	0.80	0.85	Negative
II	Hypophysial tumour (adiposogenital syndrome)..	0.64	0.60	0.51[1]	0.70	Slight anxiety
III	Hypophysial tumour (adiposogenital syndrome. Polyuria).....	1.20	1.00	0.90	0.95	Negative

[1]Patient had some chocolate. We have already published details of this case (20).

In any case, the contradictions observed may be explained by the error, to which we all as physicians are inclined, of comparing data obtained under totally different conditions (organisms of different kinds, spontaneous or experimental syndromes, different techniques used in obtaining the data, etc.).

But we may consider as a definite conclusion that, in the regulation of the carbohydrate metabolism, the hypophysis can be classified in the group of "endocrine factors producing hyperglycemia" together with the suprarenal and thyroid glands, and consequently antagonistic to the "endo-

crine factors producing hypoglycemia'' represented principally by the pancreas, and perhaps by the gonads and parathyroid glands. Before proceeding, we wish to state that we purposely refer to ''the hypophysis'' as a single organ, although it is probable that each of its three portions exercise different endocrine functions, yet, as Biedl (21) has remarked, in practice we have not yet adequate data for attributing specifically to the various parts the phenomena which we observe in the human clinic.

As we have stated previously, our experience has shown that the hyperglycemic effect—rarely glycosuric—of the hypophysis extract on the human organism is frequent (but not absolutely constant) and its intensity varies according to the different pathological conditions. Also the period of appearance and development of this hyperglycemia varies in each case. In order to determine these details with precision, we have established a clinical test which consists in determining the blood sugar with the patient fasting, and then at intervals of 30, 60 and 90 minutes after an injection of 2 cc. of a hypophysial extract, which was always the same and was tested and proved active. Our previous experience with normal subjects has shown that under these circumstances the full development of the post-pituitary glycemia curve, and consequently the pathological variations, can be faithfully observed.

In all cases we have followed the technique of Folin and Wu.

The number of subjects observed, and of service for our object, was 44. The results obtained are set forth in the following tables:

TABLE IV

NORMAL ADULTS

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I		0.85	0.92	0.95	0.92
II		0.95	0.98	0.93	0.95
III		0.91	0.94	0.91	0.90
VI		0.80	0.90	0.83	0.81
V		0.90	0.96	0.95	0.90
VI		0.82	0.85	0.82	0.82

TABLE V

DIABETES MELLITUS

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Severe diabetes	2.24	2.34	2.32	2.24
II	Severe diabetes	2.70	2.90	2.84	2.84
III	Slight diabetes	1.90	2.10	1.95	1.95
IV	Slight diabetes	1.80	1.80	1.83	1.80
V	Slight diabetes	1.55	1.80	1.80	1.56
VI	Medium diabetes	1.80	1.83	1.80	1.90

TABLE VI
DIABETES INSIPIDUS

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	No hypophysial symptoms	1.12	1.12	1.16	1.16
II	No hypophysial symptoms	1.50	1.60	1.60	1.58
III	No hypophysial symptoms	1.50	1.68	1.57	1.57
IV	No hypophysial symptoms	1.03	1.11	1.20	1.15
V	No hypophysial symptoms	1.10	1.19	1.19	1.18

TABLE VII
TYPICAL ACROMEGALY

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Typical acromegaly	0.77	1.20	0.96	0.90
II	Acrom. and intermittent glyc.	1.33	1.33	1.50	1.79
III	Typical acromegaly	1.10	1.25	1.34	1.33
IV	Typical acromegaly	0.77	1.10	0.97	0.85
V	Acrom. and intermittent glyc.	1.38	1.79	1.78	1.78
VI	Typical acromegaly	1.04	1.20	1.27	1.33
VII	Typical acromegaly	0.90	0.99	1.28	1.35
VIII	Typical acromegaly	1.00	1.00	1.28	1.35
IX	Acrom. and ovarian insufficiency	0.83	0.82	0.82	0.81

TABLE VIII
HYPERPITUITARISM

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Acromegaloid syndrome	0.80	0.96	0.95	0.90
II	Acromegaloid syndrome	1.00	1.05	1.06	1.34
III	Acromegaloid syndrome	1.00	1.00	1.25	1.33
IV	Acromegaloid syndrome	0.75	0.75	1.00	1.50

TABLE IX
NON-HYPERFUNCTIONAL HYPOPHYSIAL SYNDROMES

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Hypophysial infantilism	0.80	0.80	0.82	0.81
II	Hypophysial tumour	1.33	1.50	1.66	1.50

TABLE X
OTHER ENDOCRINE DISTURBANCES

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Addison's disease	0.75	0 80	0.81	1.00
II	Hyperthyroidism	0.93	1.25	1.27	1.27
III	Ovarian insufficiency	0.95	1.06	1.06	1.11

TABLE XI

AFFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Epilepsy	0.73	0.75	0.76	0.73
II	Epilepsy	0.85	0.93	0.85	0.84
III	Post-encephalitic syndrome	1.32	1.35	1.70	1.68
IV	Cerebral syphiloma	0.72	0.76	0.74	0.72

TABLE XII

OTHER DISEASES

Case	Diagnosis	Blood Sugar (fasting)	Blood Sugar After Injection of 2 cc. Hypophysial Extract		
			30′	60′	90′ After
I	Pellagra	0.98	1.02	1.02	1.50
II	Recklinghausens' disease	1.14	1.16	1.14	1.14
III	Pulmonary tuberculosis	0.85	0.96	0.95	0.95
IV	Pulmonary tuberculosis	0.78	0.90	0.86	0.82
V	Tuberculosis spondylitis	0.80	0.82	0.86	0.82

Examination of the preceding data shows that in the majority of both normal and sick individuals, the injection of pituitrine produces a slight increase of the blood sugar, which usually attains its maximum about half an hour after the injection, and returns to its original value one hour or sometimes one hour and a half afterwards. In certain cases this decrease reaches below the original figure.

But evidently the intensity of the pituitrinic hyperglycemia varies according to the different pathological conditions. In a certain group, precisely the hyperpituitary patients, this hyperglycemia usually attains figures which are higher than in other abnormal states. Occasionally this post-pituitrinic hyperglycemia does not appear until after the first hour.

If, now, we calculate the average glycemic increase in each of the groups of diseases of the above tables, we obtain the following extremely demonstrative data:

TABLE XIII

AVERAGE PITUITRINIC HYPERGLYCEMIA IN FOLLOWING DISEASES

I	Hyperpituitarism	+37.0 mg.
II	Typical acromegaly	+31.8 mg.
III	Other endocrine disturbances	+25.0 mg.
IV	Non-functional hypophysial lesions	+17.5 mg.
V	Other diseases	+16.6 mg.
VI	Diabetes mellitus	+14.6 mg.
VII	Lesions of the central nervous system	+12.5 mg.
VIII	Diabetes insipidus	+11.6 mg.
IX	Normal adults	+ 5.9 mg.

It is evident from this table that the pituitrinic hyperglycemia attains more than +30 mgm. in cases of hypophysial hyperfunction, either of the typical acromegalic form, or as more or less openly declared hyperpituitar-

ism. It is exceptional when the hyperglycemia reaches this figure in the other groups of diseases, and always remains much lower in the normal organism.

Individual examination of the cases increases the demonstrative value of these average figures. If we admit +30 mgm. as the characteristic of what we may call the *positive reaction,* it will be seen that this occurred in all except one (observation IX) of the cases of acromegaly (Table VII), and this exception might be explained, perhaps, by the concomitance of a state of intense ovarian insufficiency. In the cases of hyperpituitarism (Table VIII) the reaction was lacking in only one (observation I), which refers to an adult suffering from intense cephalalgia, pronounced development of the skeleton and an evidently extended sella turca.

From Table IX we observe that the reaction was negative in the hypophysial infantilism (observation I), through a pituitary lesion of the hypofunctional type. On the other hand, it was positive in the case of a patient suffering from amaurosis due to a hypophysial tumor, revealed by x-rays (observation II); we suspect, however, that this case, in which the basal metabolism was high, corresponds to others which we have published (22) of hypophysial tumors with latent hyperfunction, which does not give place to the acromegalic symptoms until long afterwards.

In one case of hyperthyroidism (Table X, observation II) the reaction was positive, and seems to indicate the relationship between the hyperglycemic tendency of hyperthyroid and acromegalic patients. We have therefore decided to continue this investigation on our hyperthyroid patients. On the other hand, in all cases of diabetes mellitus (Table V) the reaction was negative and confirms the opinion of those who differentiate between pancreatic hyperglycemia and other glandular hyperglycemias.

The pituitrin hyperglycemia reaction was constantly negative in insipid diabetes (Table VI), in contradiction to Tingle and Imrie (23), who observed an enormous increase of the glycemia half an hour after the injection of pituitrine in a base of this disease, which figure fell to normal shortly afterwards. These authors describe a case of decrease of the post-pituitrin glycemia in diabetes mellitus, and, as we have seen above, this has not been confirmed by our experience.

In a case of post-encephalitic parkinsonism (Table XI, observation III), we obtained a very positive reaction, which may perhaps be explained by the localization of the lesion in the diencephalo-hypophysial system. This hypothesis does not, however, agree with the negative results observed in the diabetes insipidus, in which the lesion is topographically similar, but it may be that the functional type is not the same in one case as in the other.

In a case of pellagra (Table XII, observation I), there was a high but belated hyperglycemia. The latter figure, which we were unable to repeat, induces us to suspect that it might have been due to some technical error.

In a case of Addison's disease (Table X, observation I), we observed a rather accentuated, but belated, reaction: +25 mgm. This does not coincide with the results of certain investigators, as Fritz (11), who suggests that the experimental extirpation of the suprarenal gland prevents the pituitrin hyperglycemia. On the other hand, it confirms Nitzescu's conclusions (24), that the pituitrin hyperglycemia is not fundamentally altered in animals intoxicated with ergotamine, and consequently deprived of excitability of the sympathetic system.

Our results are not authoritative enough to allow us to take part in the discussion now proceeding as to the mechanism of the pituitrin hyperglycemia. We would, however, draw attention to the fact that the scanty effects observed by us in diabetic patients seem to oppose the opinion of many that there is a direct antagonism between the hypophysial incretion and the pancreas incretion. If such antagonism existed, the pituitrine would accentuate the hypoinsulinemia of diabetic patients, and consequently the hyperglycemia and glycosuria. As stated above, our observations coincide with the opinion of those who consider the pituitrin glycosuria as belonging to the group of "extra-insulinar glycosurias." On the other hand, we are under the impression (through lack of experience we cannot form a conclusive opinion) that insuline is less efficacious in the glycosuria of acromegalic patients than in the case of pancreatic diabetes. Several other authors, amongst them Ulrich, recently (25) are of this same opinion.

Our investigations with Jimena and Moya (26), which coincide with those of Castex and Schteingart (27), show that the hyperglycemic action of pituitrine has no relationship with parallel modifications of the basal metabolism, since the latter, although it increases in some cases after the injection of pituitrine, is not modified in the same cases as the glycemia; in brief, it does not increase specifically in hyperpituitary patients, as does the glycemia.

The most interesting conclusion of our observations is the possibility of applying the examination of the post-pituitrinic glycemia curve to the diagnosis of the hypophysary states, and particularly hyperfunctional states. If the reader will again turn to our tables, it is not necessary to emphasize this point. Parisot (28) proposed the use, for diagnosis of hypophysial diseases, of the alterations of the carbohydrate metabolism after the administration of 300 grams of glucose, followed by the injection of 1 cc. of hypophysial extract. Examination of the glycemia curve, with the patient fasting, as we determine these values, appears to us to be more correct and demonstrative, amongst other reasons, because it eliminates the modifications of the glycemia inherent in taking the glucose, and which may appear under the influence of factors which are independent of the functional tone of the pituitary gland.

SUMMARY

Examination of the glycemia curve following on the injection of 2 cc. of hypophysial extract when fasting, and determining the blood sugar level each half-hour for an hour and a half after the injection, shows us that both in normal and sick subjects a hyperglycemic state is produced which usually attains its maximum after about half an hour, and returns to its original fasting value after another hour.

This pituitrine hyperglycemia is of an average of 5 mgm. in the normal organism, and attains superior values, which are very variable, in different pathological states.

In explicit or larvate hyperfunctional states of the hypophysis, this hyperglycemia attains higher figures than those observed in other diseases (average 30 mgm).

Thus an increase of 30 mgm. above the fasting blood sugar level may, in doubtful cases, direct the diagnosis towards hyperpituitarism. But it must be borne in mind that other pathological factors, which modify the usual shape of the glycemia curve, may coincide with the hypophysial alteration.

BIBLIOGRAPHY

1. Cushing: The Pituitary Body and Its Disorders. 1912. Philadelphia.
2. Davidoff and Cushing: Arch. Int. Med. **39**: 751. 1928.
3. Yater: Arch. Int. Med. **41**: 883. 1928.
4. Bauer: Innere Sekretion. 1927. Berlin.
5. Shapiro and Kliatshko: Arch. Neurol. & Psychiat. **15**: 85. 1926.
6. Marañon: Las enfermedades de la Nutricion y las glandulas de secrecion interna. 1920. 3 edition, Madrid.
7. Hines, Leese and Boyd: Am. J. Physiol. **81**: 27. 1927.
8. La Barre: Compt. rend. Soc. de biol. **97**: 1416. 1927. Ibid. **98**: 330.
9. Nitzescu and Benatato: Compt. rend. Soc. de biol. **98**: 58. 1928.
10. Nitzescu and Ramneatu: Compt. rend. Soc. de biol. **97**: 1105. 1927.
11. Fritz: Arch. f. d. ges. Physiol. **220**: 101. 1928.
12. Clark: Am. J. Physiol. **64**: 324. 1928.
13. Houssay: Trabajos del Instituto de Fisiologia de la Universidad de Buenos Aires. 1925-1928.
14. Pikkat: J. Med. Biol. Moscow. **4**: 40. 1927. Cited in Endokrinologie, **2**: 214. 1928.
15. Burn: J. Physiol. (London) **57**: 318. 1923.
16. Houssay and Magenta: Compt. rend. Soc. de biol. **97**: 596. 1927.
17. Olmsted and Logan: Am. J. Physiol. **66**: 437. 1923.
18. Geiling, Campbell and Ishikawa: J. Parmacol. & Exper. Therap. **31**: 247. 1927.
19. Marañon: Presse méd. **37**: 1021. 1929.
20. Marañon: Presse méd. **33**: 1665. 1925.
21. Biedl: Endokrinologie, **2**: 241. 1928.
22. Marañon: Trabajos del Servicio de Patalogia Medica del Hospital General. Vol. II, Madrid, 1928; Vol. III, Madrid, 1929.
23. Tingle and Imrie: J. Physiol. (London) **62**: (Proc.) ii-iii. 1926. Ref. in Endocrinology, **11**: 248. 1927.
24. Nitzescu: Compt. rend. Soc. de biol. **98**: 1479. 1928.
25. Ulrich: Arch. Int. Med. **41**: 875. 1928.
26. Marañon, Jimena and Moya: Trabajos del Servicio de Patalogia Medica del Hospital General. Vol. IV. (In press.)
27. Castex and Schteingart: Compt. rend. Soc. de biol. **100**: 121. 1929.
28. Parisot et Richard: Les glandes endocrines. Leur valeur fonctionnelle, Paris, 1923.

SUMMARY

Examination of the glycemia curve following on the injection of 2 cc. of hypophysial extract when fasting, and determining the blood sugar level each half-hour for an hour and a half after the injection, shows us that both in normal and sick subjects a hyperglycemic state is produced which usually attains its maximum after about half an hour, and returns to its original fasting value after another hour.

This pituitrine hyperglycemia is of an average of 5 mgm. in the normal organism, and attains superior values, which are very variable, in different pathological states.

In explicit or larvate hyperfunctional states of the hypophysis, this hyperglycemia attains higher figures than those observed in other diseases (average 30 mgm).

Thus an increase of 30 mgm. above the fasting blood sugar level may, in doubtful cases, direct the diagnosis towards hyperpituitarism. But it must be borne in mind that other pathological factors, which modify the usual shape of the glycemia curve, may coincide with the hypophysial alteration.

BIBLIOGRAPHY

1. Cushing: The Pituitary Body and Its Disorders. 1912. Philadelphia.
2. Davidoff and Cushing: Arch. Int. Med. **39**: 751. 1928.
3. Yater: Arch. Int. Med. **41**: 883. 1928.
4. Bauer: Innere Sekretion. 1927. Berlin.
5. Shapiro and Kliatshko: Arch. Neurol. & Psychiat. **15**: 85. 1926.
6. Marañon: Las enfermedades de la Nutricion y las glandulas de secrecion interna. 1920. 3 edition, Madrid.
7. Hines, Leese and Boyd: Am. J. Physiol. **81**: 27. 1927.
8. La Barre: Compt. rend. Soc. de biol. **97**: 1416. 1927. Ibid. **98**: 330.
9. Nitzescu and Benatato: Compt. rend. Soc. de biol. **98**: 58. 1928.
10. Nitzescu and Ramneatu: Compt. rend. Soc. de biol. **97**: 1105. 1927.
11. Fritz: Arch. f. d. ges. Physiol. **220**: 101. 1928.
12. Clark: Am. J. Physiol. **64**: 324. 1928.
13. Houssay: Trabajos del Instituto de Fisiologia de la Universidad de Buenos Aires. 1925-1928.
14. Pikkat: J. Med. Biol. Moscow. **4**: 40. 1927. Cited in Endokrinologie, **2**: 214. 1928.
15. Burn: J. Physiol. (London) **57**: 318. 1923.
16. Houssay and Magenta: Compt. rend. Soc. de biol. **97**: 596. 1927.
17. Olmsted and Logan: Am. J. Physiol. **66**: 437. 1923.
18. Geiling, Campbell and Ishikawa: J. Parmacol. & Exper. Therap. **31**: 247. 1927.
19. Marañon: Presse méd. **37**: 1021. 1929.
20. Marañon: Presse méd. **33**: 1665. 1925.
21. Biedl: Endokrinologie, **2**: 241. 1928.
22. Marañon: Trabajos del Servicio de Patalogia Medica del Hospital General. Vol. II, Madrid, 1928; Vol. III, Madrid, 1929.
23. Tingle and Imrie: J. Physiol. (London) **62**: (Proc.) ii-iii. 1926. Ref. in Endocrinology, **11**: 248. 1927.
24. Nitzescu: Compt. rend. Soc. de biol. **98**: 1479. 1928.
25. Ulrich: Arch. Int. Med. **41**: 875. 1928.
26. Marañon, Jimena and Moya: Trabajos del Servicio de Patalogia Medica del Hospital General. Vol. IV. (In press.)
27. Castex and Schteingart: Compt. rend. Soc. de biol. **100**: 121. 1929.
28. Parisot et Richard: Les glandes endocrines. Leur valeur fonctionnelle, Paris, 1923.

Book Reviews

THE FUEL OF LIFE. John James Rickard Macleod. Princeton University Press, Princeton, 1928. Pp. 147.

This book summarizes much of the recent experimental evidence regarding the source of the carbohydrate oxidized by muscle tissue, some possible intermediary substances in carbohydrate oxidation, and the rôle of insulin in the process. Macleod believes that fat as well as protein is converted into glycogen before it can be used as fuel for combustion in the muscles and brings together much evidence, both direct and indirect, in support of his view.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. E. Abderhalden. Abt. V. Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus. Teil 3 B, Heft 5. Berl. & Wien., 1928. Urban & Schwarzenberg. Pp. 669-822.

This section of Abderhalden's voluminous work on biological methods is of especial interest to Endocrinologists. It is sold separately.

A section on secretion is contributed by Adolph Buckel and Carl von Eweyk. Johannes Hett writes on morphology and experimental studies on the ovary. G. L. Schkawera treats on the methods of investigating isolated organs and J. B. Collip on the preparation and assaying of parathyroid extracts.

The articles are up-to-date and authoritative.

REVUE BELGE DES SCIENCES MEDICALES. Tome I, No. 1. 1929.

This new journal that promises to be of interest and value to Endocrinologists made its initial appearance in January, 1929. It is under the editorial management of Dr. P. Lambin of Louvain. The Editorial Board consists of Professors de Beco, Bessemans, Heymans, Lemaire, Maisin and Rodhain. It is proposed to publish both original articles and abstracts of material appearing in about 25 other Belgian journals.

ESTADO ACTUAL DE LA OPOTERAPIA. E. Bonilla. "La Lectura," Madrid, 1928. Pp. 136.

In this little book Bonilla reviews in an interesting way some of the more significant literature on gland therapy. He traces the development of opotherapy through the Oriental, Greek, Roman and Medieval European periods up to the time of Brown-Séquard. He makes the interesting observation that orchitic substance was recommended as an aphrodiasic in the writings of Suskurutu as early as 600 B.C.

No attempt is made to cover the literature in detail but outstanding articles are considered from the English, French, German and Spanish

literature. The book is of especial interest in that it emphasizes the recent work appearing in Spanish.

HANDBUCH DER INNEREN SEKRETION. Ed. M. Hirsch, 1928, Bd. III, Lief. V. Curt Kabitzsch, Leipzig. Pp. 204.

Internal secretions and ear, nose and throat. Hans Leicher, pp. 1285-1413.

Internal secretions and blood diseases. H. Hirschfeld, pp. 1414-1440.

Internal secretions and the skin. K. Bingold and E. Delbaneo, pp. 1441-1488.

These three articles are useful compilations of the German literature with infrequent references to the work of other nationalities.

THYROXINE. Edward C. Kendall. The Mayo Foundation, Rochester, Minn. The Chemical Catalog Company, New York, 1929. Pp. 265.

Reviewed in Am. J. Med. Sci. **178**: 127. 1929.

SAFE-GUARDED THYROIDECTOMY AND THYROID SURGERY. Charles Conrad Miller. 1928. F. A. Davis Company, Philadelphia. Pp. 261.

This book constitutes a further addition to the now extensive list of manuals on practical goiter surgery.

The author's declared purpose is to emphasize certain phases of diagnosis and treatment that have been neglected or ignored by other writers. The volume is readable and well printed.

DIE ERKRANKUNGEN DER BLUTDRÜSEN. Wilhelm Falta. 1928. J. Springer. Wien and Berlin. Pp. 568.

A somewhat abbreviated version of this book was reviewed in this Journal, **11**: 461. 1927. The volume at hand is more satisfactory in that an index is included. So excellent and so well known to endocrinologists is Falta's book that the mere announcement of a second, fully revised, edition will suffice.

FEVER, HEAT REGULATION, CLIMATE, AND THE THYROID-ADRENAL APPARATUS. W. Cramer. 1928. Longmans, Green and Co., London. Pp. 153.

Reviewed in Physiol. Absts. **13**: 416. 1928.

PATHOLOGY FOR STUDENTS AND PRACTITIONERS. Edward Kaufmann. 1928. Translated by Stanley P. Reimann, Pathologist and Director of the Research Institute of the Lankenau Hospital. Blakiston, Phila. 3 vol. Pp. 2514.

No endocrinologist, whether he be clinician or investigator, can afford to lack knowledge of the pathology of the organs of internal secretion and the reverberations of distortions of their functions throughout the organism. In the translation of this *vade mecum* of all professional pathologists, Reimann has expanded and enlarged the original with material derived from his own experience, and included new plates, drawings, and photographs from the Lankenau Hospital service, which are a distinct addition. The

treatment of the endocrine glands is almost exhaustive, not only from the point of view of pathological anatomy, but also from the standpoint of the symptomatology which accompanies disorders of these structures. There is no question but that this enlarged edition of Reimann's is the most comprehensive and up-to-date pathology now available in English or any other language. There are many references and the work is thoroughly indexed.

DIE ERKRANKUNGEN DER SCHILDDRUSE. Professor Dr. Burghard Breitner. 1928. J. Springer, Vienna. Pp. 308.

Reviewed in J. A. M. A. **92:** 256. 1929.

GREFFE OVARIENNE ET ACTION ENDOCRINE DE L'OVAIRE, ETUDE HISTOLOGIQUE, BIOLOGIQUE, CLINIQUE, ET CHIRURGICAL. Vittorio Pettinaria. 1928. Gaston Doin & Cie, Paris. Pp. 487.

Reviewed in Am. J. M. Sc. **176:** 872. 1928.

THE SIMPLE GOITRES. Robert McCarrison. 1928. Wm. Wood & Co., New York. Pp. 106.

The material of this book, originally a Report to the International Conference on Goitre, held under the auspices of the Swiss Goitre Commission at Berne in August, 1927, is very well treated. The book has 143 excellent illustrations. Having devoted more than 25 years to investigation of the simple goitres in India, McCarrison, more than most others, is in position to clarify many phases of this chronically irksome problem in a manner both original and convincing.

Dealing with the parenchymatous or the chronic hypertrophic type of endemic goitre, the following passages illustrate the author's viewpoint: ". . . important as is a sufficiency of iodine in preventing a certain type or types of goitre, it is not a panacea for all types, nor is it proven that its insufficiency is the ultimate cause of any." Again: "Not only is iodine-deficiency held by many to be the sole cause of endemic goitre, but there are some who would seem to attribute exophthalmic goitre to this cause, unmindful of the fact that rare as iodine may be in some regions where endemic goitre prevails, exophthalmic goitre may be rarer still." Also: "It is remarkable how little attention has been paid in literature to Gaylord's important observation regarding the effect of perchloride of mercury, the tendency ever being to extol the influence of iodine, thus restricting the problem of the causation of the disease to too narrow a field." Among his many experiments, McCarrison repeatedly produced goitre in man, employing goitre-producing impure water in volunteers, himself included, and proved that out of 36 subjects 10 developed noticeable goitres. Moreover, the use of intestinal antiseptics in goitre subjects has long been shown by McCarrison to result in the cure of the disease in a goodly percentage of cases.

It is emphasized that the cause of the diffuse colloid type of endemic goitre is to be sought in factors which interrupt the normal cycle of the gland's activity at the stage of colloid storage. To look upon this type of goitre from the narrow point of view of iodine, is comparable to the mechanic who considers the efficacy of his engine solely from the point of view of lubrication. The observation of Hewer to the effect that a correlation exists between the H-ion concentration of the colloid and the secre-

tory activity of the vesicular cells is to be taken into account. McCarrison urges that we look to food deficiencies, food excesses, polluted water supplies, gastro-intestinal affections, and insanitary conditions of life, singly or in combination, as the known goitre-producing causes.

Abstract Department

On the functional activity of the adrenal gland. Cramer, W., Am. J. Physiol. **90**: 318. 1929.

Direct evidence of the functional activity of an endocrine organ can be obtained only by a method involving a microscopic technique. In fact, the conception of an internal secretion is at present based only on a theoretical postulate and not on visual demonstration. So many claims of an alleged secretory activity of the adrenal gland have failed to withstand critical examination that a few years ago several workers even raised the question whether the adrenal medulla ever does actively secrete adrenalin into the blood. A simple method has been worked out which renders visible by fixation in osmic acid vapor adrenalin as granules in the medullary cells of the resting adrenal. When the gland is stimulated to activity these adrenalin granules are seen to be expelled into the veins of the gland, giving a clear visual demonstration of "internal secretion." In this way two new facts have been elicited which have an important bearing on the mechanism of heat regulation and on the genesis of fever. 1. Exposure to cold is a powerful stimulus to the adrenal medulla. 2. Prolonged stimulation of the gland leading to a continued adrenalinaemia produces fever. These findings have since been confirmed by Boothby and Sandiford (calorigenic action of adrenalin), Aub, Cannon and their collaborators. The osmic vapor method has confirmed the secretion of adrenalin in asphyxia and in ether anaesthesia, but failed to confirm the alleged secretion of adrenalin in oxygen deficiency and after insulin which has been postulated on the basis of the indirect methods. The method has also rendered it possible to demonstrate a correlation between medulla and cortex and the existence in the adrenal gland of a mechanism which serves to inhibit the functional activity of the gland. It is urged that future investigations on the functional activity of the adrenal should be controlled by this method.—Author's Abst.

Adrenalin in fever. von Euler, U., Am. J. Physiol. **90**: 340. 1929.

Thunberg's methylene-blue method was used in the way described by Ahlgren. In the evacuated system of minced frog's muscle or rabbit's muscle and methylene-blue, with potassium phosphate as a buffer, the spontaneous oxidation-reduction was studied after addition of serum in various concentrations. Normal human serum shortened the time of decoloration, i.e., activated the oxidation, in concentrations between 1:6 and 1:400. Serum, which was taken from patients with fever or from rabbits after heat-puncture, stimulated the oxidation in the system mentioned above in concentrations as low as 1:6400-1:25,000. The same effect occurred after injection of adrenalin in man or when adrenalin was added to serum directly. This effect in connection with the sensitiveness against alkaline reaction, and the antagonism against insulin and glucose is, as Ahlgren stated, characteristic for adrenalin. The loss of the ability to get fever after adrenalectomy, which is true also for the effect of the heat-puncture (Liljestrand and Frumerie), the reactions of the adrenal glands in long-lasting fevers in connection with the statements made above support the assumption that adrenalin plays a very important rôle in fever.

—Author's Abst.

The hypoglycemic action of allylisopropylbarbituric acid (Numal) is antagonistic to adrenin (Action hypoglycémiante de l'acide Allylisopropylbarbiturique von antagonisme avec l'adrénaline). Fontés, G. and L. Thivolle, Compt. rend. Soc. de biol. **99**: 1977. 1929.

Numal reduces the hyperglycemia produced by adrenin when the two are injected simultaneously.—J. C. D.

The arterial blood pressure and the blood flow in skeletal muscles in unanesthetized cats as influenced by the intravenous injection of epinephrin. Gruber, C. M., Am. J. Physiol. **89**: 650. 1929.

Epinephrin in small doses causes a rise in blood pressure during its intravenous injection in unanesthetized cats, but this is followed by a prolonged

fall in blood pressure lasting for several minutes. In some animals only a fall is noted. Epinephrin injected intravenously in small doses in unanesthetized cats causes a dilatation of the vessels of skeletal muscles such as that observed in anesthetized animals, even though no change in blood pressure may be registered on the kymograph surface. No difference was noticed in the effect of larger doses of epinephrin in unanesthetized animals from that commonly observed in anesthetized animals. Epinephrin in large doses causes vasoconstriction of the blood vessels in skeletal muscles, simultaneously with the marked rise in blood pressure. A fall in blood pressure below the normal level is observed following the increase in blood pressure from large doses of epinephrin. Concomitantly with the fall in blood pressure, there is an increase in the blood flow from skeletal muscles.—Author's Summary.

The blood flow in skeletal muscles in unanesthetized cats as influenced by epinephrin. Gruber, C. M., Am. J. Physiol. **90:** 372. 1929.

Adrenalin chloride 0.1 to 0.5 cc. of a 1:100,000 solution injected intravenously caused either a fall, no change or a rise in blood pressure at the same time it caused an increase in the rate of blood flow from the skeletal muscle. In one animal in which epinephrin caused no increase in blood pressure the rate of blood flow increased from 42 to 72 drops per minute, returning to the control level soon after the injection. Large doses of adrenalin 0.5 to 1 cc. of a 1:10,000 solution caused a rise in blood pressure, in some cases followed by a fall. During the height of increased blood pressure a decrease in rate of blood flow from the muscle was recorded. In most cases preceding and following this decreased flow an increase in blood flow was observed. This increase was recorded even though the blood pressure fell below the control blood pressure level following the rise, e.g., in one cat 1 cc. of a 1:10,000 solution of epinephrin was rapidly injected intravenously and the arterial blood pressure increased from 133 to 250 mm. of mercury with a concomitant decrease in the rate of blood flow from the muscle from 38 to 13 drops per minute. Instead of the blood pressure falling to the normal level, it dropped to 88 mm. of mercury, a fall of 45 mm. of mercury. Four minutes were required for the normal level to be reached and maintained. Simultaneously with the sudden decrease in blood pressure the rate of blood flow from the muscle examined increased to 88 drops per minute or four times the normal rate when the blood pressure was 146 mm. of mercury. From these results we infer that there is no difference in the vaso-motor action of epinephrin on muscle vessels in unanesthetized and anesthetized cats. Since epinephrin produces a dilatation of the blood vessels in one region of the body and at the same time causes vaso-constriction in other regions, the blood pressure recorded must be that of the stronger effect minus the weaker.—Author's Abst.

The carotid sinus isolated and perfused: an area for reflex control of adrenin, output (Le sinus carotidien isolé et perfusé, zone réflexogène régulatrice de l'adrenalinosécrétion). Heymans, C., Compt. rend. Soc. de biol. **100:** 199. 1929.

By the use of three dogs, parabiotically united, it was possible to show that increased pressure in the carotid sinus reduced the adrenin output and that an increase of adrenin followed reduced pressure in the carotid sinus.—J. C. D.

Metabolism and thermo-regulation in decapsulated rats (Metabolisme et thermorégulation des rats surrénaloprives). Houssay, B. A. and A. Artundo, Compt. rend. Soc. de biol. **100:** 127. 1929.

There is a reduced heat output, shown more strikingly shortly after the operation than later. Resistance to short periods of cold is not strikingly reduced, but prolonged cold is fatal.—J. C. D.

The separation of a new physiologically active principle of the suprarenal gland. Koehler, A. E. and Lillian Eichelberger, Am. J. Physiol. **90:** 417. 1929.

An epinephrin-free substance has been separated from the suprarenal gland that is capable of elevating the basal metabolic rate and producing improvement in various types of clinical asthenias. The calorigenic activity of this substance administered to animals has proved of great value in its separation

and assay. Its preparation depends upon the separation of epinephrine and other interfering substances such as choline, its activation and finally concentration by the removal of inactive substances. Each of these processes may be accomplished in various ways. Two processes will be described, one depending upon the active principle being carried down with the protein precipitation and the other by its extraction with the lipoid fraction. Protein precipitation. The aqueous extract of the fresh glands is adjusted to pH 4-5, preferably 4.8, with acetic or other non-oxidizing acid and the protein precipitated by three-fourths saturation with NaCl or $(NH_4)_2SO_4$. This precipitate can then be washed free from the uncombined epinephrin. Such a precipitate, or its aqueous or acid extracts, however, have a depressing effect on the basal metabolism and unfavorable clinical actions. If this precipitate is protected from oxygen, the depressing action will disappear on standing and it will acquire the property of raising the metabolic rate. This change can best be accomplished by heating the precipitate with 2 to 3 M HCl on the boiling water bath for ten to fifteen minutes. The active principle can then be separated from the bulk of the protein mass by drying the acid solution in vacuo, so as to remove all moisture, extracting with absolute methyl alcohol, adjusted to pH 4.5 with ammonia in absolute methyl alcohol (pH measured by transferring small amounts of alcohol mixture to aqueous system) and precipitating with 7 volumes of acetone. Further purification can be effected by redissolving in alcohol and precipitating with acetone. Lipoid extraction. The fresh ground glands are extracted with methyl alcohol-ether mixtures, starting with 80 per cent alcohol and 20 per cent ether and gradually reversing this ratio on subsequent extractions. The alcohol and ether are then distilled off in vacuo and the water-lipoid residue extracted with ether. The separated ether extract is washed with water, dried over anhydrous Na_2SO_4 and the ether evaporated. The residue is then treated with absolute methyl alcohol containing dry HCl gas and heated on the water bath for fifteen minutes. The reaction of the alcohol solution is then adjusted, precipitated with acetone as in the protein precipitation method and similarly purified. Evidence to date indicates that the physiological effect of the substances prepared by these two methods is similar.—Authors' Abst.

Metabolic studies following the administration of suprarenal extracts. Koehler, A. E. and A. B. Hastings, Am. J. Physiol. **90**: 418. 1929.

It was found that extracts, free from adrenalin, prepared from the suprarenal gland raised the metabolism of dogs and mice when administered orally. The calorigenic effect on human subjects with a low metabolic rate is marked. These subjects exhibit a low mechanical efficiency which is raised to approximately normal by the extract. An attempt has been made to determine what factors are concerned in the alteration in metabolism. The evidence to date indicates that carbohydrates are utilized more efficiently and proteins are spared. A study has also been made of the oxygen consumption CO_2 production, and lactic acid formation by tissues excised from animals whose metabolism has been altered by various extracts.—Authors' Abst.

The effect upon the life of rabbits of the removal of the main suprarenals and the accessory suprarenal cortical tissue. Kojima, T., Tohoku J. Exper. Med. **13**: 357. 1929.

In rabbits, the metabolic rate following double suprarenalectomy shows a temporary fall, due to the operation itself, but soon returns to the pre-operative level. In double suprarenalectomized rabbits surviving for over one to two years no alteration in the metabolic rate from the normal was noticed. In these animals accessory cortical tissues were found, especially markedly hypertrophied in the cases surviving a very long time. However, in the cases where the main suprarenals and all the accessory cortical tissues were completely removed or were lacking from birth, the metabolic rate began to fall a few days before death and continued falling during the last days.—Author's Summary.

Action of tetanus toxin on the adrenal cortex (Action de la toxine tétanique sur la corticosurrénale). Mouriquand, G., A. Leulier and P. Sedallian, Compt rend. Soc. de biol. **99**: 1924. 1928.

In guinea pigs there was no effect of tetanus toxin on the cholesterol content of the adrenal cortex.—J. C. D.

The number of erythrocytes in white rats under different experimental conditions. Nice, L. B., Am. J. Physiol. **90:** 461. 1929.

Daily injections of one cc. of 1:25,000 adrenalin chloride solution administered subcutaneously into both normal and adrenalectomized white rats caused an augumentation in the number of erythrocytes in the blood drawn from the heart and this increase continued during the course of the experiment, fifty-six days. Emotional excitement produced an increase in erythrocytes in the blood of normal rats, but no change in the count of adrenalectomized or splenectomized rats. This augmentation in erythrocytes seems to come from the reservoir in the spleen.—Author's Abst.

The influence of the adrenals on the urea-forming and barrier function of the liver (Ueber den Einfluss der Nebennieren auf die harnstoffbildende und Barrierefunktion der Leber). Putschkow, N. W. and W. W. Krassnow, Arch. f. d. ges. Physiol. **220:** 44. 1928.

After adrenalectomy (dogs and cats) there is a definite increase in the amino-acid and biogenous nitrogen in blood and urine and a concurrent sharp decrease in urinary urea; such changes are identical with those following cessation of liver function or experimental removal of the liver. The biogenous amines are especially affected, and to this is to be attributed those fatal terminations in which accumulation of choline is undoubted. The isolated liver of adrenalectomized animals disposes of ammonium salts and biogenous amines more feebly than does the normal liver, and its urea output is lowered. Extract of fresh adrenals restores the barrier and urea functions of the liver. The active principle in such an extract is extroardinarily labile and is decomposed in 15 to 20 minutes. It is not adrenine and is not present in other organs.

—A. T. C.

Tetany following the use of cocaine and epinephrine in intranasal operations. Roberts, S. E., J. A. M. A., **93:** 905. 1929.

Tetany is a frequently overlooked symptom complex following the use of cocaine and epinephrine in the nose. No direct references in the literature could be found. It is not a serious complication, but a very distressing one for the patient if untreated. It is not a drug intoxication. It is not due to a condition or a single drug, but to a combination of hypoparathyroidism, hyperventilation and epinephrine in nervous, emotional patients. It is satisfactorily and quickly relieved by subcutaneous administration of parathyroid extract. (Collip).—Author's Summary.

Functions of the adrenal glands. Rogoff, J. M. and G. N. Stewart, Am. J. Physiol. **90:** 497. 1929.

It has been well established that the function of the epinephrine secretion from the adrenals is not indispensable. The important function of the glands consists of the elaboration and probably secretion of a hormone by the cortex. To distinguish this hormone from adrenalin and to indicate its origin in the interrenal tissues, we have employed the name, "Interrenalin." Marked prolongation of life has been observed by us in adrenalectomized animals when extracts of adrenal cortex were administered. Beneficial influence has been obtained, in a number of cases of Addison's disease, by administration of these cortical extracts.—Authors' Abst.

A quantitative study of human adrenals. 1. Is it possible to have a hyperfunction of adrenal tissue comparable to the hyperfunction known to exist in the thyroid gland? Schultz, W. H., Am. J. Physiol. **90:** 508. 1929.

Improved methods for assaying biologically and colorimetrically were used in studying quantitatively fresh human adrenal glands. An extensive study was made of a tumor of the adrenal gland removed from a patient diagnosed as "accessory adrenal" by virtue of the periodic hypertension amounting to as much as 260 mm. blood pressure. Extracts of this tumor compared with other fresh adrenal extracts revealed an unusually rich adrenalin content.

—Author's Abst.

Clinical experience with Addison's disease. Snell, A. M. and L. G. Rowntree, Ann. Int. Med. **3**: 6. 1929.

From the records of the Mayo Clinic about 300 definite or tentative diagnoses of Addison's disease have been made. Of these cases, 103 have been found to be authentic examples. Syphilis was present in only four patients. Of the 30 cases autopsied, 26 had tuberculosis and in four there was simple atrophy of the adrenals. The cardinal symptom, asthenia, was present in every case. Enfeebled circulation and nervous symptoms were also prominent. Pain in the back has also been a persistent symptom. Gastro-intestinal disturbances varying from mild anorexia and nausea to violent vomiting have been present in every case. Diarrhea has usually been a terminal symptom. The pigmentation is increased, due to pressure from clothing. Urinalysis usually shows that there is renal involvement. Anemia, contrary to Addison's opinion, is rare, and when it is present it is usually due to some complication. Tuberculosis was demonstrated in other parts of the body in one-third of the cases. The authors found that the triad: hypotension, hyperpigmentation and asthenia, was very suggestive of suprarenal disease. The terminal picture in Addison's disease suggests intoxication. The Muirhead treatment (epinephrine, hypodermically and rectally, and adrenal cortex by mouth) has caused temporary improvement in some cases. The pigmentation fades and the gastro-intestinal symptoms subside. The terminal symptoms did not respond to any treatment which was used. The authors believe that the patient should be protected from all tiring influences.—E. L.

On the chemistry of the adrenal cortex. Szent-Györgyi, Am. J. Physiol. **90**: 536. 1929.

The adrenal cortex contains a highly reducing substance, which is specific for the interrenal system and has been isolated as crystals. It is a hitherto unknown isomer of glycuronic acid. The substance is capable of acting as a powerful catalyst of certain biological oxidations and under certain conditions inhibits pigment formation in minute quantities (1:0,000,025 per cent). An identical substance has been isolated from peroxidase-plants. Here the substance is clearly connected as catalyst with the peroxidase system. Some chemical properties of the substance are demonstrated.—Author's Abst.

Studies on suprarenal insufficiency. IV. The blood sugar in suprarenalectomized rats. Wyman, L. C. and B. S. Walker, Am. J. Physiol. **84**: 215. 1929.

The normal blood sugar range in the rat, by the Folin micro-method is found to be from 61 to 110 mgm. per cc. whole blood, with an average value of 82 mgm. Following double suprarenalectomy, coincident with the appearance of marked symptoms of subacute insufficiency, the blood sugar values fall to between 50 and 60 mgm. In the terminal convulsive stages they may be as low as 30 mgm. In rats with chronic suprarenal insufficiency, but showing no marked symptoms, the blood sugar may fall to the lowest portion of the range of normal values and be maintained at that level, occasionally dropping below the normal low limit. In rats possessing either gross accessory cortical tissue or successful cortical transplants, in the absence of demonstrable chromaffin tissue, the blood sugar remains within the normal range. The blood sugar is normal following control blank operation, showing that the results observed after suprarenalectomy are not produced by operative trauma. The results indicate that the low blood sugar observed after suprarenalectomy is associated with cortical insufficiency. It is suggested that the cortex is concerned in the steady maintenance of a normal blood sugar level, while the medulla is an important adjunct for rapid adjustment under emergency conditions.—Authors' Summary.

Cortical and medullary factors in suprarenal insufficiency. Wyman, L. C., Am. J. Physiol. **90**: 563. 1929.

A series of studies on suprarenal insufficiency in the albino rat has been approached by using normal rats, blank operated control rats, suprarenalectomized rats having autoplastic cortical transplants but no demonstrable chromaffin tissue, and suprarenalectomized rats which exemplified all phases of suprarenal insufficiency from acute and subacute to chronic. The results have

led to the following conclusions. Increased susceptibility to histamine poisoning and to anaphylactic shock in suprarenalectomized rats is not related to cortical insufficiency, but is consequent to the lack of medullary tissue. Low blood sugar is characteristic of suprarenal insufficiency in rats and is associated with cortical insufficiency. Following double suprarenalectomy in rats the nonprotein and urea nitrogen may be increased, the amount of increase tending to parallel the severity of the symptoms of cortical insufficiency. In suprarenalectomized rats the fall of body temperature upon exposure to moderate cold and the inability to recover normal temperature rapidly is correlated with the degree of cortical insufficiency which is present. On the basis of the results of these studies and those of other investigators, it is suggested that the suprarenal cortex is concerned in the steady maintenance of certain bodily conditions, while the medulla brings about rapid adjustments in the same direction under emergency conditions.—Author's Abst.

Vagal tonus, a function of circulating adrenin (Le tonus vagal, fonction de l'adrénalinémie). Viale, G., Compt. rend. Soc. de biol. **99:** 2008. 1929.

Section of the vagus after the injection of ergotamine in dogs does not cause a cardiac acceleration. Ergotamine injected after cutting the vagus slows the heart, but increases the amplitude of the beat. Exclusion of adrenin from the circulation, by removal of one adrenal and ligation of the vein from the other, prevents the acceleration after the vagus is cut. These experiments support the author's view that circulating adrenin acts on the sympathetic endings in the heart and the vagal centers in the medulla, thereby maintaining the normal heart rhythm.—J. C. D.

Normal values of basal or standard metabolism. A modification of the duBois standards. Boothby, W. M. and Irene Sandiford, Am. J. Physiol. **90:** 290. 1929.

Basal or standard metabolic rates have been made in our laboratory on more than 60,000 individuals, up to December, 1926. From this number we have selected 6,888 subjects (1,822 males, 5,066 females) who on careful physical examination revealed no abnormalities which would influence their rate of heat production. Included in this series are the 262 school children to be reported by Sandiford and Harrington. The data are expressed on the basis of calories per square meter referred to age for both males and females, using the height-weight formula of duBois and duBois for the following reasons: 1. duBois was the first to develop a practical clinical standard of heat production. 2. The statistical treatment of our series supports the accuracy of the original duBois standards, being only 1 to 4 per cent lower for the adults and 3 to 7 per cent lower for children down to the age of fourteen. 3. The utilization of the height-weight factors combined to represent surface area and the adoption of standards on the basis of age for each sex has the great advantage of indicating simply and clearly the difference in the rate of the basal metabolism between men and women. 4. This method of expression likewise clearly shows the rapid decrease in rate of the basal metabolism of male children between the ages of five and twenty-one and the more rapid decrease in female children between the ages of five and seventeen, followed in both sexes by a gradual and nearly parallel decline to old age. 5. Finally, it permits of the correlation of the rapidly decreasing heat production from infancy to maturity and the more slowly decreasing heat production of adult life on the basis of the phenomena of intracellular motion, inevitably accompanied by increased heat formation, associated with the act of mitotic cell division.—Authors' Abst.

The influence of endocrine glands on the amount of water in striated muscle (Action des glandes endocrine sur la teneur en eau des muscles striés). Parhon, C. J., M. Kahane and V. Marza, Compt. rend. Soc. de biol. **100:** 40. 1929.

Sheep, cats and dogs, but mostly guinea pigs, were used. Thyroidectomy markedly raised the water content. A less constant and less marked rise followed spaying, castration, thymectomy, thyroparathyroidectomy, over-feeding with thymus, pregnancy, and injection with placental or cerebral lipoids. The water content was reduced by treatment after thyroidectomy, also after injection of adrenin, insulin, posterior lobe extract, and of lipoids derived from the adrenals, or the ovaries.—J. C. D.

On the regulation of the normal water-intake in rats and its experimental modification through brain punctures (Experimental diabetes insipidus). Richter, C. P. and M. E. Brailey, Am. J. Physiol. **90:** 494. 1929.

Daily water-intake was measured in 52 rats. It increased gradually with age, and was greater for the males than for the females. The gradual increase in water-intake with growth in the female as well as in the male suggested its relationship to body-weight. But body-weight was found to increase very much more rapidly than water-intake. There was, however, a perfect correlation with body-surface. At ages from 30 to 160 days all rats of either sex drank about 800 cc. per square meter body-surface per day. Various attempts have been made to modify water-intake, but only results produced by punctures made in the brain stem are reported. Lesions were made through the base of the brain with a fine scalpel in the region of the sella turcica. In 13 out of 40 animals increase in water-intake was produced. In one animal the water-intake increased from 25 cc. to 260 cc. per day, the maximum intake representing twice the animal's own body-weight. In others the increase was not so marked. The diabetic state seemed permanent, for at the time the animals were killed the water-intake was still as high as at the beginning six months before.

Authors' Abst.

Comparative influence of insulin and thyroxin on the endocrine glands (Action comparée de l'insuline et de la thyroxine sur les glandes endocrines). Watrin, J. and P. Florentin, Compt. rend. Soc. de biol. **100:** 111. 1929.

Injections of insulin cause, in guinea pigs, hyperplastic activity in the thyroid and hypophysis. Thyroxin produces loss of weight with degenerative changes, particularly in the pancreatic acinar tissue. There is an increase in the number of islands.—J. C. D.

The endocrine conditions essential for the production of deciduomas (Conditions endocriniennes de la formation de déciduomes). Brouha, L. and H. Simonnet, Compt. rend. Soc. de biol. **99:** 1926. 1928.

In rats the life of the corpus luteum can be prolonged by extracts of the anterior lobe of the hypophysis. Using this method and that of producing oestrous when desired by doses of folliculine, the authors found that typical deciduomas were produced only when the action of folliculine was followed by that of corpus luteum. Implantation of the egg they conclude depends on the consecutive action of these two hormones, not on the action of corpus luteum alone.—J. C. D.

The masculinization of capons with bull serum from the point of view of the law of special thresholds and the "all or none" law (La masculinisation des chapons par le sérum de toureau considérée a point de vue de la loi des seuils différentiels et de la loi du "tout ou rien"). Busquet, H., Compt. rend. Soc. de biol. **99:** 1855. 1928.

As in partial castration there are dosages at which the different sex characters appear. The order in which they appear with increasing dosage is not the same as that found with increasing masses of testis, crowing being the first in the former and the reddening of the comb in the latter. Within narrow limits, the law of special thresholds for each character holds in both types of masculinization. If the sex hormone available is in excess or below these narrow limits the "all or none" law holds.—J. C. D.

Folliculin from urine of pregnant women. Doisy, E. A., C. D. Veler and S. Thayer, Am. J. Physiol. **90:** 329. 1929.

A study of the extraction of folliculin from urine has shown that chloroform and olive oil are the best solvents of those tested. Using chloroform and a continuous liquid extraction apparatus, large quantities of the crude extract have been prepared. The apparatus used permits the extraction of about 30 liters of urine per 24 hours with a recovery of over 75 per cent of the hormone. The crude extract is refined according to the principles outlined below. The extraction with olive oil has proved to be quite satisfactory, about 50 per cent of

the folliculin being removed by stirring the urine for half a hour with an amount of olive oil equal to 1/20 of the volume of urine. The hormone is then transferred to ethyl alcohol, the concentration of alcohol reduced to 70 per cent with water, and the alcoholic solution extracted with petroleum ether. The alcoholic solution is distilled, the residue dissolved in butyl alcohol, and this alcoholic solution extracted with dilute sodium hydroxide. The butyl alcohol is distilled, the residue leached with ethyl ether, the ether distilled and the residue dissolved in butyl alcohol. Petroleum ether is added and the precipitate discarded. The hormone is then extracted from the butyl alcohol-petroleum ether solution with dilute acids or alkalies. Separation of the hormone from the aqueous solution and a repetition of the aqueous extraction has given a product of which 1 rat unit weighs less than 0.001 mgm. An attempt to apply the procedure described for the preparation of aqueous solutions from liquor folliculi to urines, resulted in failure. This failure of the liquor folliculi method might have been due to either (a) a difference in the contaminating substances, or (b) a chemical difference between the physiologically active substances of liquor folliculi and urine. In line with the latter possibility is the paradoxical situation of the large amount of folliculin in the blood and urine during pregnancy, yet the reports of abortion produced by injections of the oestrous hormone. Working with the highly purified preparations (1000 R. U. per mgm.), we can say that the solubilities give no reason for doubting the identity of the two products. In addition, a certain set of reactions of the hormone from the two sources with benzoyl chloride and a-naphthyl isocyanate yields the same results. Since our evidence, both chemical and physiological, points to the identity of the active material of the liquor folliculi and urine, and the simple procedure of preparation described yields a very pure product from a readily available, cheap source, clinical and experimental work with the oestrous hormone will be greatly expedited.

Irradiation of ovaries and hypophysis in menstrual disorders. Ford, F. A. and D. G. Drips, Radiology, **12**: 393. 1929. Abst., Arch. Physical Therapy, **10**: 426.

Irradiation of ovaries or hypophysis has been effective in re-establishing menstruation in patients in whom prolonged use of organotherapy had been ineffective. A conclusion cannot be drawn as to the comparative efficiency of methods because the cases selected for irradiation were of unusual severity. Irradiation of the hypophysis, occasionally combined with splenic and hepatic irradiation, has exerted a temporary regulating effect in 7 cases of severe menorrhagia and metrorrhagia; with supplementary treatment, the effect in two cases has persisted more than one year. Relief of dysmenorrhea has been incidental in certain cases of menorrhagia and oligmenorrhea. Of 6 cases treated primarily for dysmenorrhea, relief has been complete in three and has lasted for a period of four to six months; improvement occurred in two others. Irradiation of ovaries of white rats in various dosages has resulted as follows: There was no continued influence on the regularity of the estrual cycle. Complete destruction of follicles did not result from dosage up to 2.5 unit skin doses.

The sex hormones. Funk, C., Am. J. Physiol. **90**: 353. 1929.

The male and female sex hormones show far reaching analogies in their chemical behavior. Both substances can be extracted from various sources by means of chloroform and are soluble in dilute alkalies. If one subjects crude extracts to the action of alkalies, the active substances are found in the non-saponifiable fraction. We are dealing here either with fatty acids, or, which is more likely, with phenols or alcohols. The lessened activity of the sex hormones in the form of their aqueous solutions suggests a separation into two constituents, one of which is less soluble than the other.—Author's Abst.

Notes on the antagonism between the follicule and the corpus luteum (Quelques considérations sur l'antagonisme entre le follicule et le corpus jaune). Goormaghtigh, N. and A. Amerlinck, Compt. rend. Soc. de biol. **100**: 439. 1929.

Normal mice injected regularly with folliculine showed prolonged oestrous periods. The corpora lutea developed slowly and to only a slight degree. This is further proof of antagonism between folliculine and the corpus luteum.

—J. C. D.

Recent studies on transplantation of desiccated ovaries (Nouvelles observations sur la transplantation d'ovaries après dessiccation). Kallas, H., Compt. rend. Soc. de biol. **100:** 97. 1929.

In guinea pigs, the vitality of ovaries for grafts is much reduced when they have lost more than 40 per cent of their weight through drying, and entirely destroyed at 60 per cent.—J. C. D.

On the cyclic vaginal changes in spayed animals (Sur un rythme vaginal chez les animaux ovariectomisés). Kostitch, A. and A. Télébakovitch, Compt. rend. Soc. de biol. **100:** 51. 1929.

In spayed white mice the vaginal smears show cyclic changes similar to but less intense than those of normal oestrous. These are associated with changes in the cells of the vaginal epithelium, which do not, however, show the stage of keratinization characteristic of normal oestrous. Cyclic vaginal changes then are not dependent on the corpus luteum or the ovary.—J. C. D.

Results of oral administration of female sexual hormone "Menformon" (Über weibliches (sexual) hormon Menformon. Weitere Erfahrungen über Wirkung oraler Gaben). Laqueur, E. and S. E. de Jongh, Klin. Wchnschr. **7:** 1851. 1928. Abst., Physiol. Absts. **14:** 52.

To produce oestrus in rats by oral administration of "menformon" 100 times the subcutaneous dose is required. In mice 11 times the subcutaneous dose is effective when given orally. When given by the rectum, rats require 25 times the subcutaneous dose to produce oestrus. In rats, 900 mouse units produced marked growth of the uterus within 11 days. In male rats the hormone in a period of 6½ weeks retarded the growth of the genitalia. In male guinea-pigs, oral administration of the hormone caused the mammary glands to grow considerably, and in one instance they produced milk.

Transplantation of ovaries after drying (Transplantation d'ovaries après dessecation). Lipschütz, A., Comp. rend. Soc. de biol. **100:** 95. 1929.

In guinea pigs desiccated ovaries can be grafted provided the drying is not too great.—J. C. D.

Transplantation of preserved ovaries. I. Endocrine action of ovaries preserved on ice (Transplantation von konservierten Ovarium. I. Endokrine Wirkung von auf Eis konservierten Ovarien). Lipschütz, A., Arch. f. d. ges. Physiol. **220:** 11. 1928.

Ovaries kept at temperatures below 0° C. are damaged to such an extent that following transplantation only degeneration occurs. Ovaries kept at +1 to +3° for from 1 to 16 days and then transplanted (guinea-pigs) retain activity and are capable of hyperfeminizing male animals, the effect lasting for 5 months or more. Six positive results have been obtained with ovaries preserved for from 1 to 3 days, and five positive results with ovaries preserved for 7 to 16 days. Some damage results from the preservation; the proportion of successful results is less than with freshly transplanted ovaries, the latent period of action is lengthened, and the survival period is shorter.—A. T. C.

The ovarian hormone in relation to women. McClendon, J. F., C. Conklin, F. Wildebush and H. Wiles, Am. J. Physiol. **90:** 448. 1929.

From biometric analysis of 438 determinations of basal metabolism on ten women, including the calculation of the probable errors, it was shown that the basal metabolism rises during the pre-menstrual period and falls during menstruation to the lowest level during the post-menstrual period. The excretion of the ovarian hormone follows the same curve. During menstruation no ovarian hormone could be determined in the urine. During the post-menstrual period four single-injection mouse units were recovered from a 24-hour specimen of urine. During the pre-menstrual period 20 single-injection mouse units were recovered from a 24-hour specimen of urine. The hormone seemed to be present in the blood plasma during the greater part at least of the inter-menstrual

period. None was found in the corpuscles. Owing to the positive correlation between the hormone and the basal metabolism an attempt was made to raise the basal metabolism by injecting the hormone. It was found that the single-injection doses up to about 4,000 mouse units at 8:00 a. m. was followed by a very slight rise in the metabolism to 6:00 p. m., but owing to the necessity of withholding food, the metabolisms were interrupted. At 8:00 a. m., the next day there was a normal basal metabolism. The metabolism of the same subjects without injection of hormone rose slightly during the day, but not as much as with injection. By giving several injections a day it was possible to raise the metabolism still higher and also cause an increase in metabolism the following day. Women who had never menstruated showed none of the hormone in their blood. Injections of hormone were made into women who had never menstruated and who were undeveloped in secondary sexual characters and accurate measurements of the secondary sexual characters were made. In women who had menstruated but at the time had had amenorrhea of considerable duration, injection of the hormone caused menstruation to occur again.—Authors' Abst.

Thyroid tissue tumors of the ovary (with the report of an apparently toxic case). Moench, G. L., Surg. Gynec. Obst. **49**: 150. 1929.

Three cases are reported, one of which seems to have contained actually functioning thyroid tissue. Hence Bauer's assumption that cases of struma ovarii are really pseudomucinous ovarian cysts or cystadenomata ovarii is denied, and they are considered to be teratomata.—A. T. C.

The effect of bilateral ovariectomy in cats upon sensitivity to insulin. Myers, W. K., Am. J. Physiol. **89**: 610. 1929.

Bilateral ovariectomy in cats caused an immediate increase in sensitivity to insulin. There was a gradual recovery of resistance to insulin to such an extent that the sensitivity was subsequently diminished in comparison with that of the intact animal. Blood sugar levels and the general reaction to insulin did not coincide from time to time. This would suggest that insulin shock and hypoglycemia are separate and distinct manifestations resulting from the injection of insulin. There seems to be an exaggeration of their independence following the recovery of the animal from the immediate effects of ovariectomy. Bilateral ovariectomy was followed in these cats by a marked and unmistakable increase in weight.—Author's Summary.

Note on changes in testicular grafts in he goats and rams (De l'évolution des greffes testiculaires du Bouc et du Bélier). Retterer, E., Compt. rend. Soc. de biol. **100**: 168. 1929.

The grafts described were one and two years old and showed the steps in the gradual alteration and disappearance of the parenchymal cells and their replacement by connective tissue.—J. C. D.

Amblyopia recidive after operative removal of the ovaries. Rosenstein, A., Ztschr. f. d. ges. Neurol. u. Psychiat. **115**: 13. 1929. Abst., Arch. Neurol. & Psychiat. **21**: 1186.

In spite of the great frequency of female genital disorders, periodic blindness has not been reported up to the present time. Rosenstein reports a case of a woman, aged 29, who in 1926 first noted migrainous attacks with dimness of vision which occurred very irregularly. About three months later she had a total extirpation of the uterus, leaving an ovarian rest. One month after this she had blindness, lasting from three to four days, with her migrainous attacks, and thereafter she had this periodic migraine and blindness every four weeks at the time of her menses. The visual disturbances began and ended with concentric shrinking of the visual field, and with loss of color vision, only the green remaining intact. The pupils became wide, while the fundi did not show any changes in either the vessels or the nerve heads. The convergence reaction of the pupils was decreased, accommodation was not interfered with, and the external ocular muscles were not involved in the attacks. Examination of the rest of the nervous system gave negative results, and the spinal fluid was

entirely normal. Following ovarian therapy, the condition improved. The author attributes the transient blindness to a nerve rather than a retinal disturbance, and says that concentric narrowing of the visual field as seen in this case is characteristic of many diseases of the optic nerve, as, for example, in optic atrophy.

Body changes following experimental castration (Modifications morphologiques après castration expérimentale). Werner, G., Compt. rend. Soc. de biol. **100:** 47. 1929.

Young sheep and guinea pigs when castrated gain weight less rapidly than controls, while the reverse is true in adults. Castrates lose weight less rapidly in starvation. There are also body changes in the sheep after castration which involve the head and teeth.—J. C. D.

Studies on the modifications of the sugar, calcium, and urea in the blood following experimental castration (Recherches sur le modifications de la glycémie, de la calcémie et de l'urémie après castration expérimentale). Werner, G., Compt. rend. Soc. de biol. **100:** 49. 1929.

Rabbits, guinea pigs, sheep and dogs were used. There was an increase in these animals of all three substances after castration.—J. C. D.

Action of the anterior lobe extract of the hypophysis on the basal metabolism in man (Action de l'extrait du lobe antérieur de l'hypophyse sur le métabolisme basal chez l'homme). Castex, M. R. and M. Schteingart, Compt. rend. Soc. de biol **100:** 121. 1929.

Subcutaneous and intramuscular injections in man of commercial extracts of the anterior lobe raised the basal metabolic rate in eighteen cases and reduced it in seven.—J. C. D.

Secretion into the blood stream from the anterior lobe of the hypophysis in the cat (L'excrétion hémocrine dans le lobe antérieur de la glande pituitaire chez le chat). Collin, R., Compt. rend. Soc. de biol. **100:** 107. 1929.

The "black granules" seen in the sinusoids of the pituitary may be broken down red blood cells, since a drop of anterior lobe substance, obtained from fresh crushed gland, haemolyzes blood.—J. C. D.

Concerning the hypophyseal (Pars Distalis) hormones for growth and for reproductive processes. Cushing, H. and H. M. Teel, Am. J. Physiol. **90:** 323. 1929.

Experiments in this laboratory with the injection of anterior lobe extracts on dogs confirm the recent work on rats and mice (Evans, Smith) in establishing the fact that there are two distinct hormones. 1. The growth principle. Intraperitoneal injections in dogs cause in time a pathological overgrowth with splanchnomegaly, hyperplasia of thyroid and adrenal cortex in association with the following symptoms: polyphagia, polydipsia, polyuria, sialorrhea, lactation, asthenia and physical inactivity. In the females the genitalia become enlarged in the absence of oestrus; in males, testicular atrophy occurs and libido is diminished. Chemically: no elevation of the basal metabolic rate has been demonstrated; blood cholesterol tends to be elevated; no observable change occurs in serum protein, in calcium, phosphorus or sugar. It has been shown, however, that the non-protein nitrogen in the fasting blood falls approximately 25 per cent following injection of the growth principle. 2. The sex principle. Boiled dilute acetic acid extracts of very fresh bovine glands (anterior lobe), made according to the method described by Spaul (1924) for producing premature metamorphosis in salamanders, have brought about premature oestrus in twenty-six day old female rats. The ovaries enlarge though to a less extent than the enlargement produced by Smith's method of introducing living anterior lobe transplants. Not all extracts produced by this method have proved to be active, but the results make it evident that the sex principle may sometimes be present in acid extracts which invariably destroy the growth principle.

—Authors' Abst.

A comparison of anterior hypophyseal implants from normal and gonadectomized animals with reference to their capacity to stimulate the immature ovary. Evans, H. M. and Miriam E. Simpson, Am. J. Physiol. **89**: 371. 1929.

The authors determined that castration and, to a less extent, cryptorchidism, result in increase in the size of the hypophyses and in an augmentation of their ability to promote sexual development when used as transplants.
—R. G. H.

A comparison of the ovarian changes produced in immature animals by implants of hypophyseal tissue and hormone from the urine of pregnant women. Evans, H. M. and Miriam E. Simpson, Am. J. Physiol. **89**: 381. 1929.

With certain limits, the weights of ovaries stimulated to precocious development by implants of rat anterior hypophyseal tissue are roughly proportional to the amount of tissue implanted. If four times the minimal dose is given, the ovaries are increased approximately four times in weight. On the other hand, if four times the minimal extract dose be given, the resulting ovaries are not appreciably heavier. The minimum dose of extracts of the urine of pregnant women can be increased one hundred and sixty fold and the resulting ovarian tissue in the young female is barely trebled thereby. This difference in the weights of ovaries that develop as a result of implant and of extract treatment is primarily due to difference in the number of follicles stimulated. The minimal effective implant treatment stimulates a much more general follicular development than does the corresponding dose of urine extracts, where a small number on "crop" of follicles are picked out by the hormone and carried to the corpora lutea stage.—Authors' Summary.

Comparative physiology of the anterior lobe of the hypophysis (Physiologie comparée du lobe antérieur de l'hypophyse). Lipschütz, A., H. Kallas and E. Wilckens, Compt. rend. Soc. de biol. **100**: 28. 1929.

Uterine changes are produced in young mice by injection of large amounts of anterior lobe from the pigeon. This shows that the pigeon gland also contains oestrous producing substance, though to a smaller degree than the pituitaries of mammals.—J. C. D.

New experiments on the pituitary hormone and the law of puberty (Nouvelles observations sur les hormones hypophysaires et la loi de la puberté). Lipschütz, A. and H. Kallas, Compt. rend. Soc. de biol. **100**: 30. 1929.

Extracts from the hypophysis of very young guinea pigs and from a senile dog, when injected into mice, produced a characteristic, though weak, stimulation of oestrous.—J. C. D.

The pituitary gland and the suprarenal cortex. Moehlig, R. C., Arch. Int. Med. **44**: 339. 1929.

From a review of the literature it is concluded that anencephalus is accompanied by pituitary anomalies. The degree of anomaly varies in different cases, being greatest in anterior cerebral defects. The suprarenal cortex reflects the state of the pituitary gland and is always hypoplastic when the pituitary is involved in anencephalus. Hyperplasia of the pituitary gland results in hyperplasia of the suprarenal cortex. The view that cerebral defects are responsible for aplasia of the suprarenal cortex must be modified to the view that the pituitary gland is the responsible factor. It is to be emphasized that only the suprarenal cortex and not the medulla is involved in these pituitary anomalies, and the same holds true for experimental hypophysectomy. The embryohormonic relation of the pituitary to mesenchymal tissues gives a clearcut explanation of this singular involvement. The importance of the relation of the pituitary gland to the suprarenal cortex is readily realized when cholesterol metabolism is considered. Many related problems can be studied with a newer and better foundation.—Author's Summary.

Primary pituitary tumors. Puestow, C. B., Arch. Neurol. & Psychiat. **22**: 547. 1929.

In a series of 50 primary tumors of the pituitary body more than 60 per cent were adenomas. Malignant lesions were found in 16 per cent of cases. Growth stimulation, manifested chiefly by acromegaly, was not found in cases other than in those of adenoma. Amenorrhea was present in 13 of 14 cases of adenoma and in only two of six cases of malignant lesions.

—Author's Summary.

Studies in acromegaly. VIII. Experimental canine acromegaly produced by injection of anterior lobe pituitary extract. Putnam, T. J., E. B. Benedict and H. M. Teel, Arch. Surg. **18**: 1708. 1929. Abst., Physiol. Absts. **14**: 244.

This paper records the first successful attempt to produce acromegaly experimentally in higher animals. The experiment was conducted with two pedigreed, thoroughbred English bulldogs, female litter mates, aged 4 weeks. During the 3 weeks that they were kept under observation before the experiment began, they increased in weight normally and equally. On April 7, 1927, they weighed, respectively, 4.87 and 5 kgm. The lighter animal was then injected with 10 cc. of specially prepared anterior lobe extract, this being continued daily during the course of the next 14 months with gradually increasing doses, the animal receiving 75 cc. just before her death. The control animal received daily corresponding amounts of sterile saline. Within a month it was evident that the dog which received the anterior lobe substance was growing considerably faster than the control, and from then on the rate of growth was so much more rapid that she eventually acquired twice the weight of the control (45 kgm. as opposed to 23 kgm.). In addition, the animal showed enlargement of the tongue, great increase in the size of its bones, prognathism, pendulous skin, enormous hypertrophy of the mammary glands, with the production of colostrum and marked hypertrophy of the sexual organs. The animal eventually succumbed after exposure to the sun for some hours on a hot day. The control was then sacrificed and complete necropsy of both animals was carried out with microscopic study of all tissues and glands. The chief features of the necropsy were the marked signs of skeletal overgrowth with hyperostosis, generalized splanchnomegaly affecting particularly the thyroid and genital tract, adenomas of the suprarenal, and many ripe but unruptured follicles in the ovaries. The tissues of the control were entirely normal, grossly and microscopically. The observation is regarded as due to the effect of the two anterior lobe hormones of the growth-promoting and the sexual principles.

Is pituitary secretion concerned in the inheritance of body-size? Robb, R. C., Proc. Nat. Acad. Sc. **14**: 394. 1928. Abst., Arch. Neurol. & Psychiat. **21**: 1202.

A comparison was made of the weights of the pituitary bodies in giant (Flemish) and dwarf (Polish) male rabbits and in their F_1 hybrids. There is no characteristic difference in the weight of the pituitary body that may be correlated with the differences observed in growth rate. With increase in body weight, a progressive decrease in relative pituitary weight occurs. In the full-grown dwarf rabbit, accordingly, there is relatively twice the amount of pituitary substance observed in the adult Flemish giant rabbit.

The action of anterior lobe of the hypophysis on milk secretion (Action du lobe antérieur de l'hypophyse sur la montée laiteuse). Stricker, P. and F. Grueter, Compt. rend. Soc. de biol. **99**: 1978. 1929.

In rabbits, injections of anterior lobe extract produces lactation only after the mammary gland has been acted on by corpus luteum. In dogs and rabbits it will re-establish milk flow up to two weeks after weaning.—J. C. D.

The effect of extracts containing the growth principle of the anterior hypophysis upon the blood chemistry of dogs. Teel, H. M. and O. Watkins, Am. J. Physiol. **89**: 662. 1929.

The blood of fasting dogs was analyzed just before and for a number of hours after the injection of growth promoting extracts of the anterior hypophysis of the ox. During the experimental period no significant changes were found

in total phosphorus preformed or total creatinine, uric acid or sugar. A drop in serum calcium following the injection was often but not always observed. Very slight changes in inorganic phosphorus sometimes occurred, but the findings were not consistent. A marked drop in non-protein nitrogen, however, was always observed after the injection of an active extract (20 to 30 per cent). The disappearance of some urea and amino acids from the blood following injection was also an almost constant finding, the amount of drop in these constituents being fairly well in keeping with the percentage composition of the blood, and not sufficient to account for more than 70 per cent of the total drop in non-protein nitrogen. Control experiments showed that after twenty hours of fasting a level of non-protein nitrogen, urea and amino acids is reached in the blood. Pituitrin does not cause a disappearance from the blood of non-protein nitrogen, urea or amino acids. Neither does an extract of serum protein, nor an extract of anterior hypophysis which has been inactivated by boiling. These control experiments indicated that the disappearance of non-protein nitrogen, urea, and amino acids from the blood following the injections of active extracts is probably due to the effect of the growth principle of these extracts. The question arises as to whether or not this disappearance of non-protein nitrogen constituents of the blood may be attributed to increased excretion. It is impossible to draw any final conclusions upon this point, for the amounts of non-protein nitrogen and urea which disappear from the blood are too small to be traced in the urine. Experiments, however, in which the dog is deprived of water, thus cutting down on urine formation, still show appreciable drops in the non-protein nitrogen constituents of the blood after injection, and seem to furnish some evidence against increased excretion as the only explanation of the phenomena observed. Also the fact that the amino acids and the "undetermined nitrogen" portion of the blood decrease after injection seems to indicate that the effect is at least in part of an endogenous nature. The distribution between corpuscles and plasma of the non-protein nitrogen constituents of the blood is apparently not affected by the injection of active extracts of the anterior hypophysis of the ox. The disappearance from the blood of these constituents after injection is in general rather evenly distributed between corpuscles and plasma. Total analysis of the blood of two dogs who had been made definitely acromegalic by daily injections of active extracts of anterior lobe, did not reveal any definite changes in the composition of their blood from what it had been during the control period before any injections had been given. The results of the experiments carried out in the course of this investigation seem to supply some evidence that the growth promoting principle of the anterior hypophysis has an immediate effect upon the non-protein nitrogen constituents of the blood. It seems reasonable that this effect might be, at least in part, one of mobilization from the blood for the building up of new protoplasm.—Authors' Summary.

The cerebral circulation. XI. The action of the extract of the posterior lobe of the pituitary gland. Wolff, H. G., Arch. Neurol. & Psychiat. **22**: 691. 1929.

Extract of the posterior lobe of the pituitary gland causes constriction of pial arteries, arterioles, veins, venules and minute vessels. Vasoconstriction after intravenous injections of pituitary indicates that the diameter of the brain vessels is influenced more by the chemical content of the blood than by its hydrostatic pressure.—Author's Summary.

The effect of liver on the blood sugar level. Blotner, H. and W. P. Murphy, J. A. M. A. **92**: 1332. 1929.

A study of the effect of liver feeding on the blood sugar indicates that whereas previously liver has been regarded as an unsuitable article of food for diabetic patients because of its glycogen content, it is now known to have a beneficial effect on the blood sugar of these patients. The liver fractions that are effective in the treatment of pernicious anemia have no effect on the blood sugar, whereas certain liver fractions that are ineffective in the treatment of pernicious anemia have an effect on the blood sugar like that of liver. Four patients with diabetes, taking liver daily or from three to five times a week, have been observed with repeated blood sugar determinations for approximately one year, while in two, who were followed from twenty and thirty days, it was found that the blood sugar has remained at a constantly lower level than pre-

vious to liver therapy. These observations suggest that liver contains a blood sugar reducing substance active when taken by mouth, non-toxic, and with an effect on the blood sugar concentration similar to that obtained with insulin. It is difficult to estimate the quantity of liver that will replace a known amount of insulin, but we feel that 180 gm. of liver will have an effect on the blood sugar of certain diabetic patients equal to that of from 10 to 15 units of insulin. —Authors' Summary.

The compensatory or preventive action of pancreatic grafts on normal and diabetic glycemia (Action compensatrice ou préventive de la greffe pancréatique sur la glycémie diabétique ou normale). Houssay, B. A., J. T. Lewis and V. G. Foglia, Compt. rend. Soc. de biol. **100:** 140. 1929.

Extra pancreatic material grafted into normal dogs did reduce the blood sugar, but not below normal limits, regardless of the size or number of the grafts.—J. C. D.

Effects of pancreatic grafts on variations in glycemia produced by glucose injections (Action de la greffe pancréatique sur les variations de la glycémie produites par l'injection de glucose). Houssay, B. A., J. T. Lewis and V. G. Foglia, Compt. rend. Soc. de biol. **100:** 142. 1929.

The blood sugar curve showing a rise and return to normal produced in unoperated dogs by injection of glucose is likewise seen in depancreatized dogs carrying pancreatic grafts. The innervation is, therefore, not essential to the increatory action of the pancreas.—J. C. D.

Effects of large doses of insulin on the blood pressure (Action des fortes doses d'insuline sur la tension artérielle). Jung, L. and L. Auger, Compt. rend Soc. de biol. **99:** 1989. 1929.

In dogs, large doses of insulin produce a considerable reduction in blood pressure, which, however, appears slowly.—J. C. D.

Some effects of long continued insulin administration in rats. Lee, M. O., Am. J. Physiol. **90:** 427. 1929.

The effects of continued insulin administration were determined on voluntary activity, blood count, growth, heart rate and oestrous cycle in rats. Insulin was injected twice daily in dosages of 0.1, 0.5 and 1.0 units per 100 grams body weight. Voluntary activity was measured by the revolving cage method with 25 rats. Two periods of one month each with insulin were alternated with two periods of one month without. The voluntary activity was slightly increased during the periods of insulin administration. In 20 rats blood examinations, consisting of erythrocyte, leucocyte and differential leucocyte counts, were made. The only deviation in the insulinized rats was a slight increase in eosinophile cells. Growth was slightly accelerated during the first four months of life in a series of 16 insulinized rats as compared with controls. The heart rate in 10 insulinized adult rats averaged 10 per cent lower than the rate in normal animals, when determined 12 or more hours after the last doses of insulin. In normal rats the administration of insulin in doses insufficient to produce convulsions, caused within 2 hours a decrease of 15 to 20 per cent in the heart rate. This decrease was abolished by atropine. These results are interpreted as due to stimulation of the parasympathetic system by insulin, and point towards an antagonistic relation of insulin and adrenalin. The oestrous cycles in insulinized rats were found to be normal, both as to the total duration of the cycles and the duration of the component stages.—Author's Abst.

The relation of the liver to the action of insulin. Murlin, J. R., H. B. Pierce and D. E. Gregg, Am. J. Physiol. **90:** 458. 1929.

This problem has been studied in three ways: 1, in vitro, employing incubation and aseptic technique; 2, perfusion of the liver; and 3, treatment of dogs having pancreatic diabetes. Under the first method attention has been centered on the proportion of true sugar to non-sugar reducing substances with and without the addition of insulin, before incubation, after incubation for

from 2 to 24 hours, and after hydrolysis of the remaining glycogen. It has been found that the addition of some organic acids profoundly affects the distribution of the reducing substances as well as the total amounts recoverable after incubation and hydrolysis. With the second method it has been shown that with proper precautions there is no demonstrable transformation of fat to carbohydrate in the perfused liver. With the third method, it has been found that the absorption of insulin from the alimentary tract of the depancreatized dog is materially enhanced by various liver products; as bile, salt solution suspension of liver pulp and some extracts. We are inclined therefore to the belief that the favorable effects of liver pulp on diabetes reported by Blotner and Murphy are due to insulin already present in fresh liver, its absorption being aided in certain individuals by bile or its precursors and possibly by some extractive substances.—Authors' Abst.

The placental transmission of insulin from fetus to mother. Pack, G. T. and D. Barber, Am. J. Physiol. **90:** 466. 1929.

Insulin is transmitted through the placenta of the goat from fetus to mother, as determined by variations in maternal blood-sugar levels following intrafetal injection of commercial insulin. The experiments were carefully controlled by the previous determinations of glucose tolerance under the same conditions.—Authors' Abst.

Metabolism of galactose. VIII. Non-diabetic glycosurias. Rowe, A. W. and Mary McManus, Am. J. Physiol. **90:** 502. 1929.

In a series of over three thousand cases correlation studies have been made between the tolerance for galactose, blood sugar levels, and the appearance of a spontaneous glycosuria. The relationship of blood sugar levels and glycosuria in diabetes is contrasted with the same observations in large groups presenting several endocrine and non-endocrine disorders. Analysis of these demonstrates the complexity of the mechanism regulating carbohydrate metabolism and the complete independence of many spontaneous glycosurias from blood sugar levels. Pituitary, thyroid, and ovarian cases presenting certain aberrant functions show glycosuria with normal or low sugar levels, while in disease of the adrenals (Addison's) a glycosuria is frequently observed with blood sugar levels even below a low normal. Of the non-endocrine factors various injuries to the central nervous system, hepatic disorders, syphilis, primary anaemia, and the leukaemias all show a fairly frequent incidence of glycosuria, with only exceptionally a blood sugar level above the conventional normal. The anomalous carbohydrate metabolism during pregnancy is also considered, and the existence of a renal glycosuria discussed.—Authors' Abst.

Studies on sugar regulation by means of the tolerance for insulin (L'étude de la glycorégulation par le test de tolérance a l'insuline). Sendrail, M., Compt. rend. Soc. de biol. **99:** 1901. 1929.

The responses of normal individuals to very small doses of insulin are variable, but fall within fairly definite limits. Reactions outside these limits are a clue to pathological conditions.—J. C. D.

The utilization of carbohydrate by totally depancreatized dogs, receiving no insulin. Soskin, S. and W. R. Campbell, Am. J. Physiol. **90:** 524. 1929.

Totally depancreatized dogs, in which the absence of islet tissue was subsequently verified by post-mortem examination, have been maintained without insulin for as long as four weeks. Fed on protein alone, these animals lose weight steadily, but remain bright and active throughout most of the experiment. For one to two weeks after cessation of insulin administration the animals exhibit an R. Q. of 0.700 or less. The D:N ratio, which starts off at high levels, has frequently fallen below 2.00 by the end of the first week. The ketosis, as judged from urinary excretion, reaches its height about the fourth or fifth day, then steadily declines. During the remaining one to three weeks of the experiment, the R. Q. steadily rises to values as high as 0.900. During this time, the CO_2 combining power and CO_2 content of the blood are not appreciably diminished, and may even rise. The D:N ratio continues to fall, fre-

quently to levels less than 1.00. If insulin be now cautiously resumed, the animal may be revived. It gains weight steadily, and subsequent determinations will again start off with "diabetic" R. Q.'s and D:N ratios. The addition of fifty grams of glucose to the regular diet, from time to time during the latter half of an experiment, results in the retention of a progressively increasing amount of the administered glucose. The glucose retention, often as much as 60 per cent, is accompanied by a variable effect on the R. Q., and a definite lowering of the urinary nitrogen and ketone excretion.—Authors' Abst.

Insulin in the treatment of pernicious anemia (L'application de l'insuline dans le traitement de l'anemie pernicieuse). Varga, V., Paris méd. **19:** 249. 1929.

Eight cases of pernicious anemia were treated with insulin and liver extract with highly beneficial results. In particularly severe cases with anorexia, where there is difficulty in taking liver, treatment with insulin is particularly indicated.—M. O. L.

Diabetes mellitus. Woltman, H. W. and R. M. Wilder, Arch. Int. Med. **44:** 576. 1929.

Diabetic neuritis is mainly a sensory disturbance without corresponding motor impairment; pain paresthesia and areflexia are its main characteristics. It shows also a marked predilection for the lower extremities. The histologic material from 10 cases studied clinically is described. Two of these cases are instances of diabetic polyneuritis. In these two cases, isolated bundles of nerve fibers were necrotic. The degeneration noted in the spinal cord is relatively unimportant, and it is doubtful whether it could explain the clinical data. The lesions in the spinal cord no not resemble those found in combined degeneration of the cord seen in pernicious anemia. The most significant lesions are those of the nerve trunks. These are associated in nearly all cases with marked thickening of the walls of the intraneural vessels. The degeneration is more marked toward the periphery. There is good reason to believe that neither glycosuria nor acidosis plays a direct part in the production of diabetic neuritis. In the 10 cases studied, syphilis could be diagnosed in only one, and other complicating infections and intoxications, such as those caused by alcohol and certain metals, were not sufficiently in evidence to explain the neuritis. The results of this study lend support to the opinion that the factor of greatest significance in the lesions of the nerves found in diabetes mellitus is atherosclerosis.

—Authors' Summary.

Parathyroid therapy in schizophrenia. Bowman, K. M., J. Nerv. & Ment. Dis. **70:** 353. 1929.

In 3 cases of catatonia parathormone was given in the hope of lessening the rigidity. Light doses of calcium lactate, as well as thyroid substance, were also used in some of the experiments. Neither the blood calcium nor the catatonic symptoms were significantly influenced.—R. G. H.

Co-relation of calcium metabolism, parathyroid function and chronic pulmonary tuberculosis. Ellman, P., Tubercle **10:** 257. 1929. Abst., J. A. M. A. **92:** 1390.

Ellman states that the calcium content of the blood serum in pulmonary tuberculosis varies only within normal limits; namely, from 9 to 12 mgm. per 100 cc. The supposed diminution of the calcium content of the blood in pulmonary tuberculosis found by some observers has not been confirmed during the course of this work. In cases responding favorably to treatment the calcium content can be raised, but only within normal maximum limits. The object in view, therefore, in treatment with calcium or parathyroid therapy, is to endeavor to raise the blood calcium to its maximum concentration point. The administration of calcium or parathyroid must be continued over a prolonged period if calcium retention is to be promoted. A combination of parathyroid extract with calcium lactate has proved as effective as any. Microscopic examination of the parathyroid glands in cases of pulmonary tuberculosis shows signs of increased functional activity of the glands. Hence, the conclusion is reached that there is a definite relationship between pulmonary tuberculosis on the one hand, and calcium metabolism and parathyroid function on the other.

The diuretic action of the parathyroid extract. Hueper, W. C., Arch. Int. Med. **44**: 374. 1929.

During the course of experiments with dogs receiving injections of parathyroid extract, it was observed that this hormone has a strong vagotonic effect, evidenced by a decrease of the pulse rate, prolongation of the systole, shortening of the diastole, hyperemia of the vessels of the abdominal organs, and intensification of the peristalsis of the stomach and intestine. When the amount of the injected parathyroid extract was adjusted in such a way that the blood calcium level was raised to about 15 mgm. in 100 cc. of blood, a markedly increased excretion of urine was noticed. Dogs killed during this stage, on histologic examination of the kidneys, showed that the blood vessels, especially the glomerular capillaries, were extremely distended with blood. There were no other changes observed in the kidney, especially no tubular degenerations or calcium precipitations.—R. G. H.

Carbohydrate metabolism in parathyroidectomized dogs. Reed, C. I., Am. J. Physiol. **84**: 230. 1929.

The response of normal and parathyroidectomized dogs to the ingestion of 2 grams of dextrose per kgm. of body weight has been investigated. Dextrose tolerance curves show a characteristic response during attacks of tetany, indicating decreased tolerance. Symptoms are abated after dextrose ingestion or injection. Tolerance tests by intravenous injection give identical results, therefore, an intrinsic mechanism is involved. Intravenous injections of concentrated dextrose solutions will protect dogs during the acute stage and prolong life, but will not prevent the appearance of myotonic symptoms. During tolerance tests the following changes in blood constituents occurred: Calcemia was usually slightly decreased in normal, and non-tetanic animals. In tetany, the decrease was slightly greater. Phosphemia was generally decreased in normal and non-tetanic animals. In tetany, there was always a more pronounced decrease. The Ca:P ratio was always increased. When symptoms were completely abated the final value was above one. These results are believed to indicate an involvement, possibly indirectly, of carbohydrate metabolism in tetany. The fasting level of glucemia was not affected by the operation or the occurrence of tetany.—Author's Summary.

Carbohydrate metabolism in parathyroidectomized dogs. Reed, C. I., Am. J. Physiol. **90**: 490. 1929.

After parathyroidectomy, there is no particular disturbance of fasting glucemia, but when such animals are in tetany, ingestion of dextrose induces a curve of tolerance characterized by a progressive increase and delayed recovery during observation periods of two to three hours. Dextrose ingestion or injection tends to alleviate symptoms of tetany, causing a decrease in inorganic phosphorus and a less pronounced decrease in calcium, thus inclining toward an increase in the calcium:phosphorus ratio. Insulin produced, in normal and non-tetanic dogs, an increased calcemia and decreased phosphemia. When dogs were in tetany, insulin produced characteristic curves of hypoglucemia and hypophosphemia, but calcemia responded much less regularly, any increase being followed by a decrease. Symptoms were usually abated following insulin administration.—Author's Abst.

The excretion of calcium through the intestine in parathyroidectomized animals. Taylor, N. B. and A. Fine, Am. J. Physiol. **90**: 539. 1929.

Using an improved technic, it was found that calcium excretion by the intestine was much augmented in dogs by parathyroid extirpation.—R. G. H.

Effect of the thyroid-parathyroid apparatus on hyperthermia following injections of adrenin and of salt solution (Influence de l'appareil thyroparathyroïdien sur l'hyperthermie consécutive a l'injection d'adrénaline ou de solutions salines). Viale, G. and J. Kurie, Compt. rend. Soc. de biol. **99**: 2010. 1929.

After thyroparathyroidectomy, dogs show no rise in temperature following adrenin or NaCl. If the parathyroids alone are destroyed, there is the loss of thermal response. This indicates that it is the parathyroids which are the essential organs.—J. C. D.

The influence of the thyroid and parathyroid glands upon inorganic salt metabolism. Aub, J. C., W. Bauer and F. Albright, Am. J. Physiol. **90:** 270. 1929.

Three individuals were studied. 1. A normal man who was given sufficiently large doses of parathyroid extract to raise the blood calcium level to 12.5 mgm. per 100 cc. 2. A myxedematous woman who was given enough thyroid extract to raise her basal metabolic rate to normal. 3. A woman with exophthalmic goiter who was cured by the surgical removal of her thyroid. Calcium, phosphorus, and total base were determined in both urine and feces, and the urine excretion was analyzed for sulphur, chlorine, and titratable acidity. These subjects received daily the same food, which was inadequate only in calcium. Daily injections of 100 units of Collips' parathormone raised the blood calcium level to 12.5 mgm. per 100 cc., lowered the blood phosphorus level, and increased the urinary calcium and phosphorus excretion. Thyroid administration markedly increased calcium excretion in the myxedematous case without affecting the blood calcium level. The exophthalmic goiter patient excreted 300 per cent more calcium than normal. The effects of these internal secretion variations upon other factors of inorganic salt metabolism were surprisingly slight, and the variations that did occur were in large part due to changes in the nitrogen balance. Thus, the changes in fixed base metabolism are largely adjustments derived from the bone salts.—Authors' Abst.

Thyroid and cerebral activity. II. Vagus, thyroid apparatus and chronaxie of the sigmoid gyrus (Thyroide et activité cérébrale. II. Pneumogastrique, appareil thyroïdien et chronaxie du gyrus simoide). Cardot, H., J. Régnier, D. Santenoise and P. Varé, Rev. franç. d'endocrinol. **7:** 185. 1929.

The authors have studied the relation of the thyroid gland to cerebral irritability by determining the chronaxie of the sygmoid gyrus (Lapicque technic) before and after section of the vagus innervation of the gland. The chronaxie increases, conversely, stimulation of the vagus fibres lowers the chronaxie. The effects as determined in dogs are evident within a few minutes after nerve section or stimulations.—R. G. H.

The distinction between metabolic and nervous symptoms in thyroid disorder. Goodwin, G. M., Am. J. Med. Sci. **178:** 83. 1929.

Six cases reported emphasize the distinction between symptoms resulting from disturbance of the metabolic and of the nervous mechanism of the body. The rôle of the thyroid in the production of metabolic disorder is obvious. The nervous disorder which, for the most part, represents a disturbance of the autonomic nervous system may be either the cause or the result of thyroid disturbance. There is no reason to believe that disorders of the autonomic system may not result from other agencies than faulty thyroid secretion. The recognition of this fact is important because of the frequency with which a clinical picture made up of nervousness, tremor and tachycardia presents itself. A diagnosis of hyperthyroidism, when these symptoms are present without definite increase in metabolism, should be made with a great deal of reluctance. This is especially important as regards the nervous adolescent girl with a goiter who is often diagnosed and sometimes operated upon for Graves' disease, if minor elevation in metabolism is present.—Author's Summary.

Thyroneural dystrophy. Kraus, W. M., S. Brock and P. Sloane, Am. J. Med. Sci. **178:** 548. 1929.

Two cases are described of a condition defined as thyroneural dystrophy. It is a familial and probably congenital disorder of neuromuscular control of central origin, consisting of any or all of the following: chorea, athetocis, static fits, rigidity, ataxia, abnormal reflex changes, postural defects, and signs referable to disturbed function of the vegetative nervous system, associated with a variable degree of mental and thyroid defect. The condition may be so severe as to imitate precisely advanced cases of cerebral diplegia. Nystagmus, squint and stuttering may be present. No specific pathology is known beyond changes in the internal structure of the cells of the nervous system and a deposit of calcium and iron about the blood vessels. It seems probable that there is a

common but unknown cause of both the thyroid and neural dystrophy. It is well known that a normal thyroid gland is necessary for the development of a normal central nervous system; hence, when thyroid gland is administered early in cases of thyroneural dystrophy, the disorders due to the thyroid defect during growth may disappear. In this type of case, thyroid-gland administration is apt to be most beneficial. Reference is made to the possibility of a superimposed toxi-infectious neural involvement due to the letting down of the blood-cerebrospinal fluid barrier for colloids, in consequence of the thyroid insufficiency. Such an hypothesis may explain the late appearance of the nervous symptoms and the ineffectiveness of thyroid therapy.—Authors' Summary.

Influence of blood, blood serum, and milk on the serum calcium and the symptoms in animals after thyroparathyroidectomy (Action du sang, du sérum sanguin et du lait sur la symptomatologie et la sérocalcémie des animaux thyroparathyroïdectomises). Parhon, C. J. and Hélène Derevici, Compt. rend. Soc. de biol. **100**: 37. 1929.

In thyroparathyroidectomized dogs, milk injected intraperitoneally had some ameliorating influence and raised the blood calcium, while blood and blood serum was without effect.—J. C. D.

Thyroid size in the sexes. Riddle, O., Am. J. Physiol. **90**: 495. 1929.

Weights were obtained on the thyroids of 1917 healthy ring doves and on 602 healthy common pigeons aged 4-36 months. Within these age limits there is little or no change in body weight, and in many of the 71 races or strains studied there is little or no change in thyroid weight. The large influence of the hereditary factor in thyroid size, and many well-known physiological factors, have here been adequately equalized or controlled; but thyroid weight nevertheless shows itself to be highly variable. Mean values obtained from the union of all (71) comparable races of ring doves indicate an excess weight (per unit body weight) in the females of 4.5 per cent, or of 1.8 per cent. This mean for 19 races of common pigeons is 7.0 per cent. In general, those races which have the smallest thyroids show the smallest percentage sex difference in thyroid size; in races characterized by large thyroids, the female glands exceed those of the males by a notably higher percentage. We interpret these facts as indicating that many individuals of these races have thyroid enlargements similar to those of endemic goiter; and that, as in the human, the females are more often thus affected than are the males. The rather current impression that the thyroids of human females are larger than those of males is probably supported only or mainly by data from races or regions in which thyroid size tends to be high in both sexes—but specially high in the females—because of slight or pronounced tendencies and approximations to endemic goiter; and also because of temporary enlargements of the female thyroid at certain phases of reproduction.
—Author's Abst.

Thyroxin and nutrition (Thyroxinwirkung und Ernährung). Schlossman, H., Am. J. Physiol. **90**: 505. 1929.

The increase in oxygen consumption under influence of thyroxin is largely dependent upon nutrition. In white rats it was found that any form of "one-sided" diet diminished the metabolic reaction to thyroxin.—Author's Abst. (translated).

The endocrine toxic epilepsy. Sereisky, M. I., Collected Papers, Psychiatric Clinic of the First Moscow State University, **2**: 185. 1927. Abst., Arch. Neurol. & Psychiat. **22**: 610. 1929.

Epilepsy is often associated with disturbances of the glands of internal secretion. The thyroid gland especially has been mentioned often as being involved in the etiology of various convulsive disorders. The most common form of involvement of the thyroid in epilepsy is connected with hypothyroidism. In a fairly large series, a definite diminution in weight of the thyroid gland up to 20 gm. has been observed. Hypothyroidism in connection with epilepsy is rare. Association of epilepsy with exophthalmic goiter or of the latter with epilepsy is infrequent. Epilepsy may appear before the onset of exophthalmic

goiter, and at times hyperthyroidism precedes the onset of convulsions. The third manner in which hyperthyroidism and epilepsy are associated is when both these conditions appear approximately at the same time. It is in this group of cases that the author is especially interested, and he reports four such. In all these cases there was a history of epileptic personalities among the ancestors. Even before the onset of epilepsy the patients were described as having been extremely egocentric and temperamental, having rigid personalities of the type usually described as "epileptoid." The author believes that there is probably some relation between the two, and postulates a hypothesis that the same toxic factor which caused epilepsy also caused the appearance of the exophthalmic goiter.

Influence of thyroidectomy and parathyroidectomy on the passage of material from blood to cerebro-spinal fluid (Effet de la thyroïdectomie et de la parathyroïdectomie sur le fonctionnement de la barière hémato-encéphalique). Stern, L., L. G. Belkina, and A. O. Zlatowierow, Compt. rend. Soc. de biol. **99**: 536. 1928.

In cats and rabbits, removal of the thyroid was followed after 10 days by a change, which permitted colloids but not crystaloids to pass into the fluid, although normally neither will pass from blood to fluid. Heavy doses of fresh thyroid in normal cats gave the reverse effect. Within two days following thyro-parathyroidectomy in cats, both colloids and crystaloids pass from the blood to the cerebro-spinal fluid.—J. C. D.

Heart-block, auricular flutter, and adenoma of the thyroid. Strauss, A. E., M. Clin. N. Amer. **11**: 487. 1927.

This is the report of a case of thyroid adenoma of 5 years' duration in a woman of 39 years. The basal metabolic rate and other clinical features at first indicated thyroid hyposecretion, but later, during thyroid administration, a distinct picture of hyperthyroidism presented itself. From the beginning there were evidence of heart-block. Electrocardiographic studies revealed the presence of marked auricular flutter with continuation of the heart-block; the auricular rate being 340, the ventricular 42. Thyroidectomy resulted in the disappearance of both thyroid toxemia and auricular flutter.—I. B.

Effective range of iodine dosage in exophthalmic goiter: Preliminary report. Thompson, W. O., A. G. Brailey and Phebe K. Thompson, J. A. M. A. **91**: 1719. 1928. Abst., A. M. A.

An attempt has been made by the authors to determine the effective range of iodine dosage in exophthalmic goiter. In 12 of 13 patients at rest in bed in a hospital, as great a reduction in basal metabolism was obtained with 1 drop of compound solution of iodine (about 6 mgm. of iodine) daily as with much larger doses. In 8 of 12 patients more recently studied under the same conditions, half a drop of compound solution of iodine (about 3 mgm. of iodine) daily was as effective as were larger doses. Three patients showed no response to any dose, and one showed slightly a lower metabolic level during the administration of 30 drops daily. The minimum dose that will produce a maximum reduction in basal metabolic rate has not yet been definitely determined. It appears in most cases, however, to be between about one-fifth drop of compound solution of iodine (1.3 mgm. of iodine) and about 1 drop (6.3 mgm. of iodine) daily. There are observations which suggest, but do not prove conclusively, that the minimum dose is perhaps a little less when a patient is at rest in bed in a hospital than when the same patient is at home occupied with her daily routine.

The cerebrospinal fluid in myxedema. Thompson, W. O., Phebe K. Thompson, Esther Silveus and Mary E. Daily, Arch. Int. Med. **44**: 368. 1929.

The concentration of protein in cerebrospinal fluid (lumbar) is high in most cases of myxedema and usually drops to within normal limits following the administration of desiccated thyroid. The concentration of protein in cerebral fluid also appears to be high, although less than that in lumbar fluid. Owing to the high concentration of protein in the cerebrospinal fluid, myxedema

may, in rare instances, be confused with tumor of the brain. The ratio of the chloride content of the spinal fluid to that of plasma is often less after the administration of desiccated thyroid. The rate of flow of cerebrospinal fluid is not less, and may be greater after the administration of thyroid.

—Authors' Summary.

Pharmacological studies on thyroxin (Estudios farmacologicos sobre la teroxina). Velasquez, B. L., Arch. de med., cir. y espec. **30**: 97. 1929.

It was found that neither thyroxin nor cholin gave typical thyroid curves with guinea pig uterus, but such curves were secured by a combination of the two. Since the thyroxin must be administered first, it is supposed to be the sensitiser.—B. C.

Effect of thyroxin on vagus excitability (electric) in the frog's heart (Action de la thyroxine sur l'excitabilité électrique de l'innervation parasympathique du coeur de la grenouille). Waldenström, deJ., Compt. rend. Soc. de biol **99**: 1681. 1928.

Thyroxin solution does not modify the responses of the isolated frog's heart to vagus stimulation.—J. C. D.

The blood supply of the thyroid gland with special reference to the vascular system of the cretin goiter. Wangensteen, O. H., Surg. Gynec. Obst. **48**: 613. 1929.

The alteration in the disposition of the smaller blood vessels in goiter is intimately related to and dependent on the changes in the connective tissue stroma in which the vessels run. In adenomatous goiter, where such changes are common, deviations from the normal size and distribution of the interlobular follicular and capillary vessels are frequent. In the goiter of the cretin, where degenerative changes are especially prevalent, transition from the normal arrangement of these smaller vessels is particularly likely to obtain. Degenerative changes in the vessal walls of arteries of all orders are common in adenomatous goiters. The large extraglandular vessels so frequently seen in cretin goiters represent a compensatory attempt to insure a good blood supply to a benign neoplastic process of a hypofunctioning tissue, in which the alterations in the stroma have made a normal nutrition impossible. In areas of cretin goiters where no departure from the normal is present in the quality and quantity of the connective tissue stroma, giant capillaries may be present in the interfollicular network. Less frequently, such dilated capillaries are also observed in non-cretin adenomatous goiters. The vascular system of the goiter of cretins is not peculiar to cretin goiters alone. Its counterpart, though in less degree, is observed in the vessels of ordinary adenomatous goiters. With its biologically inert tissue, the goiter of the cretin is not able to eke out of its abundant blood supply a nutrition sufficient for normal function.—A. T. C.

On the biology of iodine and iodine combinations. von Wendt, G., Am. J. Physiol. **90**: 554. 1929.

The results of the last survey of goiter in Finland, together with a plan and the preventive measures already taken, were presented to the XIIth International Physiological Congress at Stockholm. Of the two suitable ways, the one of the direct iodine administration was applied only in a small degree. The indirect method, in which animals were fed a weak iodized fodder, seemed more promising for a country in which the use of milk and milk products is very great. Comparative research showed that this weak iodized mixture of mineral salts, having a composition such that the main defects of the mineral combinations of the usual fodder were corrected, had exercised a favorable influence on the quantity of milk as well as on the fat content of the milk. This favorable result has induced a more extensive use, so that the quantity of one million kgm. of iodized nutrient mixture, which is quite considerable for Finland, will probably be exceeded this year. Continuing the research after the Stockholm congress, a very wide increase of goiter among the domestic animals, especially the pigs and horned cattle, was observed. In districts with much human goiter only few of the calves were without goiter. On one of the estates for experi-

menting we found 72 per cent of the calves with goiter before administration of the iodized mineral salt; after a year of application to the milk cows the number decreased to only 2 per cent. Also an immediate application of the iodized mineral salt mixture to calves with goiter had a good result.

—Author's Abst.

Exophthalmos following operation for the relief of hyperthyroidism. Zimmerman, L. M., Am. J. Med. Sci. **178**: 92. 1929.

Eight cases are reported in which thyroidectomy for the relief of hyperthyroidism was followed by the development of exophthalmos. If some exophthalmos was present at the time of operation, it increased materially afterward. In every case the patients were completely relieved of thir symptoms of hyperthyroidism, and the basal metabolic rate was brought to normal or below by the surgical removal of the gland. In three of the patients the eye change was limited to one eye; in the remainder, it was bilateral. Conjunctivitis, chemosis and edema of the lids frequently accompanied the exophthalmos. The postoperative exophthalmos developed with a falling basal metabolic rate, was associated in most instances with subnormal metabolism and sometimes with frank myxedema, and was not accompanied by any other symptom of hyperthyroidism. Thyroid medication or the withholding of it seemed to have no effect on the ocular changes. No definite explanation is offered for this apparently paradoxical phenomenon, though pertinent observations are discussed.

—Author's Summary.

Annual Index

Authors

Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden. Abt. V. Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus. Book Review.....373

— (Wertheimer): Studies on action of thyroxine on animal organism and especially on the heat regulation of warm blood animals 106

— — The condition of thyroxine in the animal organism..513

Adams, M. A.: cf. Himwich.....305

Adamson, G. L. (Cameron): Preoperative treatment of Graves' disease by combination of iodized fatty acid and vitamins A and D.107

Adlersberg, D. (Porges): High carbohydrate diet in under-nourished diabetics.....503

Akiyama, S.: Influence of tubercular toxin upon the suprarenals of albino rats.....399

Albright, F.: cf. Aub.....595

Alexieff, A. A. (Joukoff): Experimental investigation on bodies of Kurloff.....298

Allen, E.: Effects of ovariectomy upon menstruation in monkeys.298

— Precocious sexual development from anterior hypophysis implants in a monkey.....298

Allen, F. M.: Present results and outlook of diabetic treatment..416

Allen, R. E.: cf. Shepardson.....492

Ambrose, C. D.: Constipation treated with pituitrin.....499

Amerlinck, A.: cf. Goormaghtigh.584

Anderson, Evelyn M.: cf. Shepardson 188

André-Thomas: Sympathetic affections and diabetes. Absence of the pilomotor reflex in localized areas 304

Andrews, E. (Reuterskiold): Danger in the postoperative use of insulin 503

Archer, B. W. C.: cf. Worster-Drought 224

Aricesco, C.: cf. Paulian.....403

Aron, M.: The function of the pancreas in tadpoles. Functional correlation between the thyroid and internal secretion of pancreas in tadpoles.....104

Artundo, A.: Effect of lowered temperature on adrenalectomized rats 399

— Metabolism of rats after adrenalectomy 399

— cf. Houssay 578

Ascheim, S. (Zondek): Diagnosis of pregnancy by detection of hormone of anterior lobe of hypophysis in the urine.....405

— cf. Zondek 503

Asimoff, G.: Conditioned reflexes in thyroidectomized animals....107

— (Lapiner): The fate of the thyroid hormone in the organism of hyperthyroidized mammals 514

Athias, M.: Results of castration in turkeys 220

Aub, J. C. (Bauer and Albright): Influence of thyroid and parathyroid glands upon inorganic salt metabolism 595

Auger, L.: cf. Jung.....591

Awrounin, H.: Case of fatty atrophy following insulin injections.503

Azérad, E.: Spontaneous hypoglycemia 503

de Azevedo, A. P.: cf. Torres....488

Bacaloglu, C. (Strugariu): Studies on glycemia and glycosuria in normal and diabetic cases...504

Baker, Lillian E. (Carrel): Effect of liver and pituitary digests on the proliferation 302

Barber, D.: cf. Pack.....592

Barber, D. J.: cf. Larson..... 63

Bardier, E.: Failure to respond to adrenin in different types of failure and death of the heart....215

Bargeat: Traitement de goitre simple (Book Review).....484

Bartlett, W. M.: The effect of hypodermic insulin on the fasting blood sugar in normal and diabetic subjects in relation to percentage normal weight.....104

— Treatment of diabetes with special reference to accessory forms of treatment.....504

Bast, T. H. (Supernaw, Lieberman and Munro): Studies in exhaustion due to lack of sleep. V. Effect on the thyroid and adrenal glands with special reference to mitochondria.....405

Bauer, H. (Loewe): The effect of synthetic thyroxin on the normal thyroid gland 420
Bauer, W.: cf. Aub.....595
Beard, S. D. (Clark and Moses): Standardization of liver extract.415
Beck, Harvey G.: The Laurence-Biedl syndrome: Report of two cases in one family: Results of treatment 375
Belawenetz, S.: Effect of thyroid administration upon the testes of the albino rat.....298
Belkina, L. G.: cf. Stern.....597
Bendixen, P. A. (Lamb): Malignant tumors of the adrenal in children with report of a case.. 97
Benedict, E. B.: cf. Putnam.....589
Benetato, Marie: cf. Nitzescu....519
Benjamin, H.: Changes in hair following vasoligation 406
Berblinger: Die innere sekretion im lichte der morphologischen forschung (Book Review).....484
Bergeim, O.: cf. Larson..... 63
Berkson, J.: cf. Flexner.....517
Biasotti, A.: Influence of suprarenals on blood pressure regulation 399
Biedl, A.: Concerning the active materials of ovary.....493
Bierry, H. (Kollmann): External activity of pancreas and islets of Langerhans during hibernation 304
—— Is endocrine function of pancreas located solely in islet tissue? 304
Bijlsma, U. G.: Influence of pituitary extract on water and salt excretion 411
Binet, L. (Kaplan): Increase of blood platelets by spleen contraction caused by adrenalin...296
Bingold, K. (Delbaneo): Internal secretions and the skin (Book Review) 574
Blaisdell, E. R.: Unusual increase of carbohydrate tolerance in case of juvenile diabetes.....504
Blanco, J. T.: Histology of the ovary in amenorrhea.....299
Bloom, J. C.: An intensive study of the thymus.....419
Blotner, H.: Use of insulin in outpatient department 504
— (Murphy): Effect of liver on blood sugar level.....590
Blumgart, H. L.: cf. Campbell.302, 411
Bochkareff, P. V. (Chernosatonska): On the influence of the removal of thyroid gland, gonads, and spleen upon the formation of agglutinins in active immunization by thyroid bacilli...297
Bochkareff, P. V. (Chernosatonska): On the influence of the removal of thyroid gland, testicle, and spleen upon the titer of the hemolytic ambocepter in active immunization 297
Bodo, R. (Marks): Relation of synthalin to carbohydrate metabolism 504
—— The action of insulin on the perfused mammalian liver.504
Bonilla, E.: Estado actual de la opoterapia (Book Review).....573
— (Moya): Sedimentation time in endocrinopathies 406
Boothby, M.: cf. Beuel.....227
Boothby, W. M. (Sandiford): Normal values of basal or standard metabolism. Modification of Du-Bois standard 582
Borchardt, E. (Dingemanse, de Jongh and Laqueur): On the female sexual hormone, menformone, especially on menformone as the hormone causing the growth of the mammal.....406
Borchardt, L.: Konstitution und innere sekretion (Book Review).484
Borg, J. F.: Diabetic acidosis: an etiologic factor in the production of auricular fibrillation...304
Borysiewicz, A.: Contraction of the spleen and changes in the splenic blood produced by adrenin injection in animals.....485
Bourget, J.: The failures of Roentgen therapy in hypophyseal tumors 411
Bourne, G.: Heart-block influenced by inspiration in a case of Graves' disease 514
Bouysset, C.: cf. Ravault.....487
Bowcock, H. M.: Diabetes mellitus in the negro race: A study of one hundred consecutive cases.505
Bowman, K. M.: Parathyroid therapy in schizophrenia.....593
Boyd, J. D. (Nelson): Growth studies of children with diabetes mellitus 505
Brailey, A. G.: cf. Thompson....597
Brailey, M. E.: cf. Richter.....583
Bram, I.: Types of Graves' disease 164
Brambell, F. W. R.: The development and morphology of the gonads of the mouse. Part III. The growth of the follicles....221
Brehme, T.: Hypophyseal "Geographical skull" 499
Breitner, B.: Die Erkrankungen der Schilddruse (Book Review).575
Britton, S. W.: Neural and hormal factors in bodily activity. Prepotency of medulliadrenal influence in emotional hyperglycemia 215
Brock, S.: cf. Kraus.....595

Brougher, J. C.: Coagulation time in parathyroid tetany.....419
— The value of acterol (irradiated ergosterol) in the treatment of thyroparathyroidectomized dogs 227
— Treatment of parathyroid tetany with cod liver oil and yeast 419
Brouha, L.: Is there an antagonism between the water soluble extract of anterior lobe and folliculine? 102
— (Hinglais and Simonnet): Notes on a new hormonal test for pregnancy 494
— (Simonnet): Action of liposoluble extracts of testis on the female genital tract.....494
— — Endocrine conditions essential for production of deciduomas 583
— — On the mode of action of certain extracts of anterior lobe of hypophysis.....500
— — Regulation of contracting uterus by hormones.....221
Brown, S.: cf. Fine.....106, 419
Brownell, K. A.: cf. Hartman...401
Bruch, H.: Investigations on gas metabolism in recovery from exercise in healthy and sick children 107
Brunn, H.: cf. Pearl..... 98
Brush, N. H.: cf. Manning.....496
Bugbee, E. P. (Simond): Bio-assay of preparations of ovarian follicular hormone 407
Burge, W. E.: cf. Verda..... 46
Burn, J. H. (Ling): Effect of insulin on acetonuria.....505
Burr, G.: cf. McClendon.....300
Burwash, Frances M.: The iodine content of the thyroid of two species of elasmobranchs and one species of teleost.....514
Busquet, H.: Masculinization of capons with bull serum from the point of view of the law of special thresholds and the "all or none" law 583
Butler, E. G.: The thyroid and the rate of cell division.....308

Caccuri, S.: Effect of ligature of pancreatic ducts on the regulation of the glycogen titer.....225
Cameron, A. T.: cf. Adamson....107
Campbell, D.: cf. Geiling.....416
Campbell, J. R. (Blumgart): The treatment of diabetes insipidus with pituitary posterior lobe extract applied intranasally..302, 411
Campbell, W. R.: cf. Soskins....592
Campos, F. A. de M. (Cannon, Lundin and Walker): Conditions affecting capacity for prolonged muscular work.....399
Candido de Oliveira, J.: cf. Coelho.505
Cannon, W. B.: cf. Campos.....399
Cardot, H. (Regnier, Santenoise and Varé): Thyroid and cerebral activity. II. Vagus, thyroid apparatus and chronoxie of the sigmoid gyrus 595
— (Régnier, Santenoise and Vidacovitch): The vagus and the thyroid 514
Caridroit, F.: Can the testis produce female plumage in spayed domestic hens? 494
— Results of total ligation of the testicular pedicle in the domestic cock 494
Carmichael, E. A.: Case of disappearance of subcutaneous fat following subcutaneous injections of insulin.....505
Carrel, A.: cf. Baker.....302
Carson, D. A. (Dock): The effect of iodin upon experimental hyperthyroidism in man.....107
Cartland, G. F.: cf. Payne.....300
Carulla Riera, V.: Effect of roentgen rays on disturbances of thyroid function 514
Cassuto, A.: Experimental histology and clinical observations on the destruction by chemical means of the sympathetic of the spermatic cord 99
Castex, M. R. (Schteingart): Action of adrenin on calcium, potassium, and metabolic rate in normal cases and those with thyroid disorders 485
— — Action of the anterior lobe extract of hypophysis on basal metabolism in men.587
— — Effects of guanidine derivatives in diabetes.....305
del Castillo, E. B.: Effect of splenectomy and pinealectomy on the oestrous cycle in white rats.494
— Oestrous cycle in adrenalectomized rats 485
— Reappearance and character of the oestrous cycle following ovarian grafts in spayed white rats 494
Caylor, H. D.: Suprarenal-renal heterotopia 215
Cervera, L. (Torres-Carreras): Some reflections on a case of dystrophia adiposo-genitalis....181
Chagas, E.: Adrenal syndrome in yellow fever 485
Chalfant, S. A.: Clinical manifestations of ovarian dysfunction..296
Chambers, W. H.: cf. Himwich...305
Champy, C. (Morita): Selective growth of adult plumage in chicks treated with thyroid....515
Chang, H. C. (Ma): Further observations on tryptophan and the thyroid gland 515
— cf. Lim 403
— cf. Tung 104
Chernosatonska, E. P.: cf. Bochkareff 297

Chernosatonska, E. P.: cf. Preobrashensky 310
Chidester, F. E. (Eaton and Thompson): Influence of desiccated suprarenal cortex and medulla on growth and maturity of young rats 485
— cf. Eaton 485
Chio, M.: Action of adrenalin on the isolated heart.....216
Choay, A. (Choay): The action on diabetes insipidus of powdered posterior lobe of hypophysis...102
— — Treatment of diabetes insipidus by nasal doses of powdered pituitary lobe.....412
Choay, L.: cf. Choay.....102
Choay, Lucie: cf. Choay.....412
Christian, H. A.: Myocardial disturbances due to abnormal thyroid function and their management 107
Christiansen, Tage: Macrosomia adiposa congenita 149
Clark, G. A.: A comparison of the effects of adrenalin and pituitrin on the portal circulation.....295
Clark, G. W.: cf. Beard.....415
Clausen, Ethel M. Luce: Effect of infra-red radiation on growth of rachitic rat 308
Cobb, Ivo Geike: The glands of destiny: A study of the personality (Book Review).....848
Coelho, E. (Candido de Oliveira): Effect of ergotamine on digestive hyperglycemia in normal and diabetic subjects 505
Cohen, P.: cf. Karelitz.....104
Cole, L. J. (Hutt): Further experiments in feeding thyroid to fowls 308
Cole, W. H. (Womack): Reaction of thyroid gland to infections in other parts of body.....308
Coller, F. A.: Adenoma and cancer of the thyroid.....309
Collin, R.: La neurocrinine hypophysaire. Etude histophysiologique du complexe tubero-infundibulum-pituitaire (Book Review) 484
— Secretion into blood stream from anterior lobe of hypophysis in cat.....587
Collier, J. S.: Thyroid neoplasm with secondary deposits in skull.420
Colonna, A.: cf. Pighini.....393
Conklin, C.: cf. McClendon.....300
Conklin, F.: cf. McClendon.....585
Cori, C. F. (Cori): Influence of epinephrine on blood sugar utilization of functional hepatectomized rats 295
Cori, G. T.: cf. Cori.....295
Coronedi, G.: On the synthetic thyroxin, pharmacological experiments 309
Corner, G. W.: Physiology of the corpus luteum. I. The effect of very early ablation of the corpus luteum upon embryos and uterus 221
Costolow, W. E.: cf. Soiland....520
Cotte, G.: Treatment of menorrhagia of ovarian origin with insulin 407
— (Pallot): Influence of follicular liquid from a case of nymphomania on the vaginal smear in the rat.....223
— — Note on ovarian hormone: Influence of corpus luteum on the oestrous cycle....221
— — Relation of insulin to ovulation 222
Courrier, R.: Does follicular hormone inhibit that of corpus luteum? 99
— Insulin and folliculine.....494
— Ripe follicles not essential for appearance of oestrus..... 99
— (Masse): Relation between the hormone of the corpus luteum and of the follicle. Follicular hormone can not replace that of the corpus luteum 99
Coward, Katherine H.: The influence of vitamin A deficiency on the oestrous cycle of the rat...495
Cox, H. H.: The complications of thyroidectomy 515
Cramer, W.: Fever, Heat Regulation, Climate, and Thyroid-Adrenal Apparatus (Book Review).574
— Functional activity of adrenal gland 577
— cf. Ludford 309
Craver, L. F.: Metastasis to thyroid gland from endothelial myeloma of bone; rapid regression resulting from roentgen-ray treatment 515
Crile, G. W.: Clinical studies of adrenalectomy and sympathectomy 400
— Clinical and experimental studies of interrelations of thyroid, adrenals and the nervous system 98
— Factors determining the end-results of thyroidectomy for hyperthyroidism 515
Croell, M. M.: Nerve fibers in the pituitary of the rabbit.....302
de Cruz, A.: Effect of adrenal tissue on lecithin 485
Cuenca, B. S.: Action of insulin on the capillary circulation....225
Cullen, T. S.: cf. Friedenwald...216
Cunningham, B. (Gladys Osborn): Infra-red sterility: Preliminary report 93
Curchod, E.: The various morphological alterations of the rhinopharynx in relation to the hypophyseal syndrome 102

Curschman, H.: Endocrine Krankheiten 213
Curtis, W. S.: Diabetes in twins.505
Cushing, H. (Teel): Concerning hypophyseal (Pars Distalis) hormones for growth and reproductive process 587

Daily, Mary E.: cf. Thompson...597
Danforth, C. H.: Cause of henfeathering in Campine and Bantam males 299
Dean, G. A.: cf. Hartman.....401
Deanesly, R.: A study of the adrenal cortex in the mouse and its relation to the gonads.....216
Deery, E. M.: Note on calcification in pituitary adenomas.....455
De Jongh, S. E.: cf. Laqueur....222
Delbaneo, E.: cf. Bingold (Book Review) 574
Demaria Massey, C.: Suprarenal and thyroid in relation to basal metabolism 406
Demel, R.: Experimental homeoplastic transplantation of testes.495
Derevici, Helene: cf. Parhon....423
Destree, P.: cf. La Barre.....306
Deuel, H. J., Jr. (Sandiford, Sandiford and Boothby): Effect of thyroxin on respiratory and nitrogen metabolism of a normal subject following nitrogen-free diet 227
Dingemanse, E.: cf. Borchardt...406
Dock, W.: cf. Carson.....107
Doering, C. R. (Lombard and Moore): Endemic goiter in Massachusetts 227
Dohrn, M.: cf. Steinach.....499
Doisy, E. A. (Veler and Thayer): Folliculin from urine of pregnant women 583
Dragomir, L.: cf. Urechia.....296
Dragstedt, C. A.: Observations on hemodynamic action of epinephrine 400
Dreyere, H.: The influence of thyroid preparations on the cardiac and vascular nerves.....516
Drips, Della G. (Ford): Irradiation of ovaries and hypophysis in disturbances of menstruation 222
— cf. Ford 584
Drouet (Hamel): Endocrine disturbances in infant and adolescent psychopathics. Their relation to hereditary syphilis.....490
Drury, D. W.: Headache.....220
— Syndrome-complex, Ménière....406
— Tinnitus aurium; its incidence in endocrine disorders.....490
Dumas, A. (Froment and Mercier): Hypotension following adrenin in tabetics 216
Duncan, W. S.: Relationship of hyperthyroidism to joint conditions 516
Dunhill, T. P.: Anesthesia in thyroid surgery 517
Duperie, R.: The presence of intra-thymic parathyroid islets and parathyroid-thymic masses in infants 106

Eaton, A. G. (Insko, Thompson and Chidester): Influence of suprarenal cortex and medulla on the growth and maturity of young (white leghorn) chicks..485
— cf. Chidester 485
Eddy, C. A.: cf. Geiling.....302
Eichelberger, Lillian: cf. Koehler.578
Elkourie, L. A. (Larson): Tissue changes in parathyroid tetany and in guanidine poisoning....419
— cf. Larson 309
Ellman, P.: Co-relation of calcium metabolism, parathyroid function and chronic pulmonary tuberculosis 593
Elmer, A. M. (Kedzierski and Scheps): Case of diabetes insipidus caused by hypernephroma metastasis in the mid-brain....224
Else, J. E.: Relationship of iodine to thyroid hyperplasia and function 40
Engle, E. T.: Effect of daily transplants of the anterior lobe from gonadectomized rats on immature test animals.....500
— The rôle of the anterior pituitary in compensatory ovarian hypertrophy 500
— cf. Smith 501
Ervin, D. M.: A contribution to the nature of diabetes. A mathematical derivation of the blood glucose curve 104
von Euler, U.: Adrenalin in fever.577
Evans, H. M. (Simpson): Comparison of anterior hypophyseal implants from normal and gonadectomized animals with reference to their capacity to stimulate immature ovary.....588
— — Comparison of ovarian changes produced in immature animals by implants of hypophyseal tissue and hormone from urine of pregnant women.588
— — Impairment of the birth mechanism due to hormones from the anterior hypophysis 500
— — Stimulation of placentoma reaction in virginal endometrium by treatment with anterior hypophyseal hormones 500
Evans, L. S.: Addison's disease in the negro 216

Falta, Wilhelm: Die Erkrankungen der Blutdrüsen (Book Review) 574

Faure, W.: cf. Steinach.....499
Fenger, M.: Treatment of exophthalmic goiter 517
Ferrero, J.: cf. Marañon.....408
Fine, A.: cf. Taylor.....594
Fine, J. (Brown): The influence of "Parathormone" on bone regeneration 106, 419
Fischer, S.: Gaseous metabolism in castrated man.....407
Fisher, N. F.: cf. Larson..... 63
Flemion, F.: cf. Riddle.....414
Flexner, L. B. (Berkson, Winters, and Wolman): Antitryptic titre in pregnancy and in hyperthyroidism 517
Florentin, P.: cf. Watrin.....583
Flück, W.: Statistics on Iodine-Basedow in Switzerland between the years 1922 and 1924.....421
Foglia, V. G.: cf. Houssay.....591
— cf. Lewis 591
Foldes, E.: Action of sulfur on carbohydrate metabolism 416
Fonseca, F.: Case showing underweight unrelieved by fattening with use of insulin.....217
— Emaciation and insulin. Hyperinsulinism 305
— (Trinaco): Changes in the blood sugar of normal subjects following treatment of the pancreas with x-ray. Effect of irradiating the pancreas on glycemia and glycosurea in diabetes.....225
— — Effect of insulin on the external secretion of the pancreas in a case with pancreatic fistula 505
Fontes, G. (Thivolle): Hypoglycemic action of allylisopropylbarbituric acid (Numel) is antagonistic to adrenin.....577
Ford, F. A. (Drips): Irradiation of ovaries and hypophysis in menstrual disorders 584
Ford, Frances A.: cf. Drips.....222
Fox, Edna J.: An investigation of the effect of glandular therapy on the intelligence quotient...490
Fraenkel, L.: Female sex hormone; clinical experiences with various ovarian preparations... 99
Frank, R. T. (Goldberger and McGee): Female sex hormone. IX. Possible significance of the rodent vaginal spread reaction in the male blood 495
Frankel, J. M.: cf. Wishnofsky..106
Frazier, C. H.: Pituitary cachexia.412
Frey, E. K. (Kraut): Detection and action of a circulatory hormone 490
Friedenwald, J. (Cullen): Carcinoma of the pancreas.....216
Fritz, G.: Mechanism of influencing blood sugar by pituitary extracts 103
Froment, R.: cf. Dumas.....216
Funk, C.: Chemistry of the oestrus producing hormone.....517
— Sex hormones 584
— (Harrow): Male hormone.....407
— (Harrow and Lejwa): The male hormone. II.....517

Gaddum, J. H.: Some properties of the separated active principles of the pituitary (posterior lobe) 412
Gallagher, T. F.: cf. Moore.....367
García Morán, J.: Hypothyroidism with marked abdominal plethora and polycythemia.....421
García Triviño, F.: Female sex hormones 408
Garland, J.: Some sidelights on the thymus vogue.....512
Garma, A.: Consideration of a typical case of pre-diabetes....416
— cf. Marañon 422
Garma, J.: cf. Marañon.....422
Gatenby, J. B.: The effect of x-radiation on the spermatogenesis of the guinea-pig.....495
Geiling, E. M. K. (Campbell and Ishikawa): The effect of insulin on hypophysectomized dogs.416
— (Eddy): The hyperglycemic effect of vasopressin, oxytocin and pituitrin 302
Gellhorn, E. (Gellhorn): The influence of endocrine secretions and of alkaloids on the permeability of animal membranes...491
Gellhorn, Hilde: cf. Gellhorn....491
Gibson, R. B.: Latent tolerance in diabetes mellitus. A study of the effect of high sugar diets with insulin on controlled diabetes 506
Gibson, T. E.: The diagnosis of adrenal tumors 486
Gifford, S. R.: Ocular complications of diabetes.....225
Gilbert, S.: cf. Rathery.....496
Gillespie, G. Y.: Uses of glucose and insulin in diseases of children 417
Giragossintz, G. (Mackler): The oral administration of adrenalin 88
Glaser, F.: The interrelation of the vegetative nervous system, hypercholesteremia and arteriosclerosis 220
Glassberg, B. Y.: cf. Strouse....510
Gley, E. (Hazard): Adrenal ablation and pancreas secretion....104
— — Simultaneous stimulation of the external and internal secretions of the pancreas.225
Glimm, E. (Wadehn): Ovarian hormone in yeast.....408
Goldberger, M. A.: cf. Frank....495
Goldzieher, M.: Interrenin, the hormone of the suprarenal cortex 486

Goldzieher, M. A. (Greenwald): Hemorrhage of the suprarenals in the new born infant..... 97
Goodwin, G. M.: Distinction between metabolic and nervous symptoms in thyroid disorder..595
Goormaghtigh, N. (Amerlinck): Notes on antagonism between follicle and corpus luteum.....584
Gordon, Murray B.: Endocrine consideration of Recklinghausen's disease; report of case with associated childhood myxedema.553
— Thyroid treatment of alopecia areata 107
Goslino, A. E. (Ferrero): Iodin content in the thyroid of Uruguayan cattle 517
Goss, H. (Schmidt): Calcium and phosphorous balances in rats during period of pregnancy and lactation 299
Gostimirovic, D.: Experimental overfeminizing and its effect on the sex of the offspring.....495
Grafe, E. (Meythaler): Contribution to knowledge of insulin production 506
Graham, D.: cf. Hepburn.....305
Grantenberg, R.: Insulin treatment in severe diabetes mellitus.506
Green, F. C.: cf. Verda..... 46
Greenberg, D. S.: cf. Nice.....295
Greenwald, H. M.: cf. Goldzieher. 97
Gregg, D. E.: cf. Murlin.....591
Grieg, D. M.: The cephalic metastases of suprarenal blastomata in children 486
Griffith, F. R.: cf. Hartman.....401
Griffith, F. R., Jr.: cf. Hartman..217
Gruber, C. M.: Arterial blood pressure and blood flow in skeletal muscles in unanesthetized cats as influenced by intravenous injection of epinephrin.....577
— Blood flow in skeletal muscles in unanesthetized cats as influenced by epinephrin 578
— Blood pressure in unanesthetized animals affected by "vasopressin," oxytocin, pituitary extract and other drugs.302
Grueter, F.: cf. Stricker.....589
Gsell-Busse, M. A.: Experiments on rat oestrus and influence on it of ovarian extract and bile..100
Guy, C. C.: Tumors of the parathyroid glands 511

Haberlandt, L.: Hormone of heart movement. X. Warm blood experiments with the heart hormone preparation 224
— Sterilization by ovarian hormones 100
Halsey, J. T.: Action of ephedrin on intestine and bronchi..... 99
Hamblen, Angeline D. (Joslin): Relative position of diabetes as a cause of death.....417
Hamel: cf. Drouet.....490
Handovsky, H.: Muscle chemistry under the influence of endocrine secretion and of poisons.....491
Hannan, J. H.: Further observations on adrenaline mydriasis at the menopause 401
Harrow, B.: cf. Funk.....407, 517
Hartman, F. A. (Brownell, Hartman, Dean and MacArthur): The hormone of the adrenal cortex 401
— (Griffith and Hartman): Observations upon adrenalectomized cats treated with cortical hormone 217, 401
Hartman, W. E.: cf. Hartman, F. A. 217, 401
Hastings, A. B.: cf. Kohler.....579
Haultain, W. F. T.: Ovarian extract after artificial menopause.495
— Value of ovarian extract after an artificial menopause.....299
Hazard, R.: cf. Gley.....104, 225
Hellwig, C. A.: Morphological changes in exophthalmic goiter following the use of Lugol's solution 108
Hepburn, J. (Graham): An electrocardiographic study of 123 cases of diabetes mellitus.....305
Herold, A. A.: Diabetic therapy with special reference to the newer remedies 305
Herrick, E. H.: Duration of pregnancy in guinea-pigs.....299
Heymans, C.: Carotid sinus isolated and perfused; an area for reflex control of adrenin output.578
— Variations in blood pressure in the head. Separation of the neurovascular from adrenal secretory reflex 486
Hicks, J. B.: Adenoma of the adrenal cortex 487
Himwich, H. E. (Chambers, Koskoff, Nahum, Adams): A mechanism maintaining the hyperglycemia of diabetes.....305
Hinglais, H.: cf. Brouha.....494
Hirohata, R. (Watanabe and S. Watarai): Chemical studies on endemic goiter in Formosa....108
Hisaw, F. L. (Meyer): Oestrous hormone in urine of pregnant cows 496
Hogben, L. T.: Comparative physiology of internal secretion.....213
Hohlweg, W.: cf. Steinach..... .....101, 223, 499
Holcomb, Blair: Study of blood sugar curves before and after thyroidectomy 467
Hollins, A. S.: cf. Lawrence.....307
Holzer, H.: cf. Klein.....226
Hornung, S.: Action of "glukhorment" on normal dogs.....306
— Hypoglycemic action of pancreatic extract given by mouth.306

Hoskins, R. G.: Endocrine factors in dementia praecox.....491
— (Sleeper): A case of hebephrenic dementia praecox with marked improvement under thyroid treatment 459
— — Endocrine studies in dementia praecox 245
Houda, E.: Bacterial factor in goiter 309
Houssay, B. A. (Artundo): Metabolism and thermo-regulation in decapsulated rats.....578
— (Lewis and Foglia): Compensatory or preventive action of pancreatic grafts on normal and diabetic glycemia.....591
— — Effects of pancreatic grafts on variations in glycemia produced by glucose injections 591
— (Lewis and Molinelli): Studies on the hyperglycemia following morphine injections: Rôle of the adrenals.....487
— (Molinelli): Adrenal secretion of a suprarenal gland anastomosed to the neck vessel, caused by stimulation of the splanchnic nerve or by nicotine 401
— — Effect of neurine and ephedrine on adrenal secretion.402
— — Pneumogastric nerves and adrenal secretion 402
Hueper, W. C.: Diuretic action of the parathyroid extract.....594
Hunter, D.: Case of postoperative tetany 228
Hutt, F. B.: cf. Cole.....308
Hymanson, A.: Status thymicolymphaticus 420

Ikonen, M. W. (Kusnetzowa): The thyroid and atropine.....228
Ingram, W. R.: Interrelation of pituitary and thyroid in metamorphosis of neotenic amphibians 412
Insko, W. M.: cf. Eaton.....485
Ishikawa, Y.: cf. Geiling.....416
Isola: cf. Ricaldoni.....414
Ivy, A. C. (Oldberg): A hormone mechanism for gall-bladder contraction and evacuation...220, 489

Jamieson, R. C.: Irradiation of thymus gland in treatment of psoriasis 512
Jelliffe, S. E.: The pineal body...512
John, Henry J.: A summary of the findings in 1100 glucose tolerance estimations 388
Johnston, Margaret W.: cf. Missal 304
Jolly, J. (Ferroux): The relative sensibility of normal and involuted thymus when exposed to x-ray 512
de Jongh, S. E.: cf. Borchardt...406
de Jongh, S. E.: cf. Laquer.....585
Joslin, E. P.: cf. Hamblen.....417
— (Lahey): Diabetes and hyperthyroidism 228, 506
— (White): Diabetic children...507
Joublot, J.: Relation between the number of corpora lutea in the rabbit and the degree of preparation in the uterus for implantation 222
Joukoff, N.: cf. Alexeieff.....298
Jung, L. (Auger): Effects of large doses of insulin on the blood pressure 591

Kahane, M.: cf. Parhon.....582
Kallas, H.: Recent studies on transplantation of desiccated ovaries 585
— cf.: Lipschütz 303, 588
Kaplan, M.: cf. Binet.....296
Karelitz, S. (Cohen and Leader): Studies on inhibition of insulin activity 104
Kaufman, E.: Pathology for students and practitioners. Book Review 574
Kauffman-Cosla, O.: cf. Marinesco 303
Kedzierski, J.: cf. Elmer.....224
Kendall, E. C.: Thyroxine. Book Review 574
Kennedy, D.: Operative treatment of exophthalmic and toxic goiter 309
Kenway, Florence L.: cf. Reid...191
Kepinov, L. (Petit-Dutaillis): Hyperglycemic action of blood from diabetic dog. Results of transfusion of diabetic and normal blood into animals carrying a pancreatic graft 306
— — Method of extracting hyperglycemia producing substance from diabetic blood 306
Kim, M. H.: Concerning influence of hormones of parathyroids on liver 511
King, J. T. (Patterson): Observation on menopause; effects of various ovarian preparations on symptoms of menopause and on basal metabolism 496
King, J. T., Jr.: Effects of ovarian preparations on symptoms of the menopause and on basal metabolism 408
Kisch, B.: Experiments on function of interrenal organs of selachians 97
Klein, H.: Review of work on so-called rejuvenation process.....408
Klein, O. (Holzer): Effect of insulin upon polyuria in diabetes insipidus; the combined effect of insulin and pituitrin upon water metabolism 226
Koch, F. C.: cf. Moore.....367

Koehler, A. E.: Differential diagnosis between hypothyroidism and hyposuprarenalism.....421
— Dual calorigenic activity of suprarenal gland 402
— (Eichelberger): Separation of a new physiologically active principle of the suprarenal gland 578
— (Hastings): Metabolic studies following administration of suprarenal extracts.....579
Koenigsberger, E. (Mansbacher): Therapeutic experiments with pituitrin in gastric atony of nurslings and infants.....501
Kojima, T.: Effect upon life of rabbits of removal of main suprarenals and the accessory suprarenal cortical tissue.....579
Kollman, M.: cf. Bierry.....304
Koppanyi, T.: Effect of subcutaneously injected epinephrin in normal human subjects..... 98
Kornfeld, W. (Nobel): Studies in myxedema. VII. Another year of individual dosage treatment in thyroid therapy in childhood and juvenile hypothyroidism...422
Koskoff, Y. D.: cf. Himwich.....305
Kostitch, A. (Télébakovitch): Cyclic vaginal changes in spayed animals 585
— cf. Radossaviyevitch 512
Kotschneff, Nina: Insulin and adrenin action on the blood sugar during the digestion period in experiments on angiotomised dogs 507
Kourilsky, R.: cf. Rathery.....496
Krassnow, W. W.: cf. Putschkow 98, 580
Kraus, W. M. (Brock and Sloane): Thyroneural dystrophy 595
Kraut, H.: cf. Frey.....490
Ksendsowsky, M., Jr. cf. Schazillo 510
Kun, H.: cf. Steinach.....101, 223
Kundratitz, K.: Thyrotoxic symptom complex in chorea minor..518
Kusnetzowa, S. M.: cf. Ikonen...228
Kylin, E.: Effect of parathyroid medication on the action of adrenalin and K and Ca content of the blood 402
Kyusaka, O.: Histological studies on corpora lutea, period of ovulation, relation between corpora lutea and cyclic changes in uterine mucous membrane, and the period of fertilization.....408

La Barre, J.: Physiological variations in secretion of insulin....418
— Sensitiveness of higher nervous centers to sugar during experimental pancreatic diabetes 306
— (Destrée): Insulin and external secretion of pancreas...306
La Barre, J.: cf. Zung..106, 418, 511
Lahey, F. H.: Crises of exophthalmic goiter 228
— Deductions from 6700 goiter operations 518
— cf. Joslin 228, 506
Lamb, F. H.: cf. Bendizen..... 97
Lanz, A. B.: Formation of adrenaline-like substance in heart..487
Laquer, F.: Hormone und Innere Sekretion 213
Laqueur, E. (De Jongh): Female (sexual) hormone 222
— — Results of oral administration of female sexual hormone "Menformon".....585
— cf. Borchardt 406
Larson, E. (Bergeim, Barber and Fisher): Influence of anterior pituitary extract on sex glands and growth 63
— (Elkourie): Tetany and blood calcium after thyro-parathyroidectomy in the goat.....309
— cf. Elkourie 419
Lawrence, C. H. (Rowe): Analysis of five hundred cases simulating endocrine disorders.....109
— — Studies of the endocrine glands; the adrenals.... 1
— cf. Rowe 231
Lawrence, R. D.: An insulin resistant case of diabetes.....417
— Studies of an insulin-resistant diabetic 507
— (Hollins): Two cases of haematuria caused by insulin treatment 307
Leader, S. D.: cf. Karelitz.....104
Leake, W. H.: The insulin treatment of diabetic coma.....508
Lee, M. O.: Some effects of long continued insulin administration in rats 591
— Studies on the oestrus cycle in the rat. IV. The basal metabolism during the oestrus cycle 100
Lehmann, J.: Question of sex-specificity of the internal secretions of the gonads. Action of secretion and alterations of pituitary of castrated rats.....100
Leicher, H.: Internal secretions and ear, nose and throat. Book Review 574
Lejwa, A.: cf. Funk.....517
Lemaire, A.: cf. Loeper.....508
Leulier, A.: cf. Mouriquand..97, 579
Lewis, D.: cf. Reinhoff.....424
Lewis, D. S. (W. de M. Scrivre): The response of chronic nephrosis to parathyroid and thyroid medication 519
Lewis, J. T.: cf. Houssay...487, 591
Lieberman, B.: cf. Bast.....405
Liljestrand, G.: cf. Von Euler...405
Lim, R. K. S. (Chang): Behavior of denervated spleen in adrenalectomized animal 403

Linder, G. C.: Two cases of diabetes treated by synthalin.....508
Ling, A. W.: Burn.....505
Ling, S. M.: cf. Tung.....104
Lipschutz, A.: New experiments on experimental hermaphroditism and the antoganism of the sex glands 496
— Transplantation of ovaries after drying 585
— Transplantation of preserved ovaries. I. Endocrine action of ovaries preserved on ice 100, 585
— Transplantation of preserved ovary. II. Endocrine action of ovaries preserved at room temperature 101
— Transplantation of preserved ovary. III. Microscopic condition of isolated and transplanted ovaries.....101
— (Kallas): Hypophyseal hormones and the "law of puberty" 303
— — New experiments on the pituitary hormone and the law of puberty.....588
— (Kallas and Wilckens): Comparative physiology of anterior lobe of hypophysis.....588
— — (Paez): Hypophyseal hormones in guinea pig.....303
Lisser, H.: Dystrophia adiposogenitalis, with atypical retinitis pigmentosa, mental deficiency, and polydactylism (the Lawrence-Moon-Biedl Syndrome).....533
— (Shepardson): A further and final report on a case of tetania parathyreopriva treated for a year with parathyroid extract (Collip), with eventual death and autopsy.....427
Loeb, L.: Structural changes which take place in the thyroid glands of guinea pigs during the process of compensatory hypertrophy under influence of iodine administration 49
Loeper, M. (Ravier and Tonnet): Action of insulin in cases of impermeable kidney in man.....508
— — Increased effect of insulin in experimental cases of impermeable kidney 508
Loeser, A.: Toxicosis of pregnancy treated with insulin.....105
Loewe, G.: cf. Bauer.....420
Loewe, S. (Voss and Paas): Experimental therapeutics of oestrous failure.....496
Lombard, H. L.: cf. Doering.....227
Ludford, R. J. (Cramer): The mechanism of secretion in the thyroid gland.....309
Lundin, H.: cf. Campos.....399
Lutaud, P.: Intracardiac injection of epinephrine in a case of later post-operative embolism and heart failure.....487
Lyon, D. M.: Synthalin in diabetes mellitus 226

Ma, W. C.: cf. Chang.....515
Marza, V.: cf. Parhon.....582
Maas, O.: Abhangigkeit der washstumsstorungen und knochenerkrankungen von storungen der inneren sekretion (Book Review) 484
— Concerning hypophyseal and chondrodystrophic dwarfs...303
MacArthur, C. G.: cf. Hartman...401
Mackler, H.: cf. Giragossintz..... 88
Macleod, J. J. R.: Fuel of life. (Book Review).....573
Maddock, S. J. (Trimble): Prolonged insulin hypoglycemia without symptoms.....226
Mahnert, A.: cf. Siegmund.....501
Mandel, L.: Suprarenal tumor with metastasis and optic neuritis...487
Manning, J. B. (Robinson and Brush): Pseudohermaphroditism (female type predominating) 496
Mansbacher, W.: cf. Koenigsberger 500
Marañon, G. (Ferrero): Action of testicular injection on chronic ulcers of legs.....408
— (Garma and Garma): Visceral projection reflexes in thyroid disease 422
— (Morros): Pituitrin hyperglycemia and its possible value in diagnosis.....564
Marine, D.: Status lymphaticus..513
Marinesco, G. (Kauffman-Cosla and St. Draganesco): Action of insulin and hypophysin on the output of urine, and especially on the carbon compounds in diabetes insipidus 303
Marmorston-Gottesman, J. (Perla): Immunologic studies in relation to the suprarenal gland.....295
Marks, J.: cf. Bodo.....504
Masse, M.: cf. Courrier..... 99
Matsumori, Tsueno: Effect of adrenalin on heart of chick embryo.537
Maurer, E.: Does fetal thyroid gland function under normal physiological conditions.....422
May, H.: Life curve of thyroid gland in goiter territory and in locality free from goiter.....310
Mazzocco, P.: Lactic acid in muscles of decapsulated rats.....218
— cf. Molinelli.....295
McCarrison, R.: Simple goiter....213
— The simple goitres (Book Review) 575
McCartney, J. L.: Dementia precox as an endocrinopathy..... 73

McClendon, J. F. (Burr and Conklin): Basal metabolism (oxygen) of normal women in relation to injection of follicular hormone 300
— (Conklin, Wildebush and Wiles): Ovarian hormone in relation to women.....585
— (Sanford): Iodine in Maryland waters in relation to goiter..310
McClenahan, W. U. (Norris): Adenoma of islands of Langerhans with associated hypoglycemia 417
McGee, L. C.: cf. Frank.....495
McGraw, A. G.: Juvenile exophthalmic goiter.....108
McManus, Mary: cf. Rowe.....592
Melamed, L.: Breakdown of the endocrine glands at the menopause and at puberty.....408
Meland, O. N.: cf. Soiland.....520
Mellanby, J.: The isolation of secretin; its chemical and physiological properties 297
Menkin, V.: Relative lymphocytosis in hyperthyroidism.....108
Menninger, W. C.: Mental disturbances associated with pituitary disorders 413
Mercier, Miss: cf. Dumas.....216
Meyer, R. K.: cf. Hisaw.....496
Meythaler, F.: cf. Grafe.....506
Michaëlis, O.: Insulin treatment of scleroderma 509
Miller, C. C.: Safeguarded thyroidectomy and thyroid surgery (Book Review) 574
Miller, J. A.: Pituitary extract in pyelitis 103
Miller, J. L.: Thyrotoxicosis from the internist's standpoint.....422
Mills, C. A.: Functional insufficiency of suprarenal glands....217
Missal, M. E. (Johnston): The failure of pituitary substances to influence the basal metabolism or the specific dynamic response to food in a normal subject.....304
Moehlig, R. C.: Pituitary gland and suprarenal cortex 588
— Pituitary tumor associated with gynecomastia 529
Moench, G. L.: Thyroid tissue tumors of ovary (with report of an apparently toxic case).....586
Molinelli, E. A.: Adrenal function of suprarenals on diphtheria intoxication 403
— Vasomotor and adrenal-secretory reaction on dogs with diphtheric intoxication 403
— (Mazzocco): On supposed existence of pro-adrenin in adrenals 295
— cf. Houssay.....487
Moll, H.: Carbohydrate diet for hyperthyroidism 423
Möller, E.: Clinical investigation into the basal metabolism in diseases of the thyroid gland.....518
Moore, Carl R. (Gallagher and Koch): Effect of testis extracts in castrated fowls and mammals.367
Moore, Fredrika.: cf. Doering....227
Moore, R. A.: cf. Spohr..... 98
Mora, J. M.: The intracutaneous salt-solution test in thyrotoxicosis 519
Morimoto, M.: Experiments on fats and lipoids in blood. IV. The partition of fats and lipoids in blood of dogs with pancreatogenic diabetes after insulin injection 226
Morita, J.: cf. Champy.....515
Morrell, J. A.: cf. Powers.....395
Morrison, H.: Familial incidence of exophthalmic goiter.....228
Morros, J.: cf. Marañon.....564
Moschini, D. G.: The effect on growth and metamorphosis of feeding ovarian tissue from normal (laying) and brooding hens to frog tadpoles.....497
Moses, M. J.: cf. Beard.....415
Mosser, W. B.: Effect of iodine and thyroid feeding on the thyroid gland; an experimental study 228
— The use of iodin in the treatment of goiter.....519
Mouriquand, G. (Leulier): The amount of adrenin in the adrenal glands in total starvation... 97
— (Leulier and Sedallian): Action of tetanus toxin on adrenal cortex 579
Moya, A.: cf. Bonilla.....406
Munro: A case of eunuchoidism..413
Munro, J.: cf. Bast.....405
Murlin, J. R. (Pierce and Gregg): Relation of liver to action of insulin 591
Murphy, W. P.: cf. Blotner.....590
Myers, W. K.: Effect of bilateral ovariectomy in cats upon sensitivity to insulin.....586

Nahum, L. H.: cf. Himwich.....305
Neligan, G. E.: Carcinoma of suprarenal 218
Nelson, M. V.: cf. Boyd.....505
Nemenow, M. (Udenburg): Radiotherapy of tumors of pituitary..413
Nice, L. B.: Number of erythrocytes in white rats under different experimental conditions....580
Back, G. T. (Barber): The placental transmission of insulin from fetus to mother.....592
— (Greenberg, Greenberg): Adrenalin and fatigability of muscle of adrenalectomized rats.295
Nitzescu, I. I. (Benetato): Inanition and glycogen in thyroidectomized dogs.....519
Nobel, E.: cf. Kornfeld.....422

Norris, G. W.: cf. McClenahan....417
Novak, E.: Present status of ovarian therapy 409

Obermer, E.: The endocrinology of tuberculosis 491
O'Brien, F. W.: Diagnosis and treatment of enlarged thymus by x-ray 420
Oldberg, E. (Walsh): The effect of colectomy on the incidence of parathyroid tetany and the blood calcium 511
— cf. Ivy.....220, 489
Olmsted, J. M. D.: Shronaxie of nerves and muscles in insulinized frogs 509
Olmsted, W. H.: Dietetic management of the diabetic in the doctor's office 509
Orel, H.: Clinical study of mongolian idiocy.....492
Osborn, Gladys: cf. Cunningham.. 93
Oslund, R. M.: Source of testicular hormone 409
Oswald, A.: The so-called condition of status thymico-lymphaticus and its relation to the endocrine system 513
Ottorino, Da Re.: The effect of the corpus luteum on the continuance of pregnancy.....497

Paas, E.: cf. Loewe.....496
Paez, R.: cf. Lipschutz.....303
Page, J. H. (Warren): Pathology of diabetes in young adults....509
Pallot, G.: On ovarian regeneration and the oestrous cycle in white rats 497
— cf. Cotte.....221, 222, 223
Parhon, C. J. (Derevici): Changes in blood chemistry in animals with hyperthyroparathyroidism and in animals following thyroid feeding 423
— — Influence of blood, blood serum, and milk on the serum calcium and the symptoms in animals after thyroparathyroidectomy..596
— (Kahane and Marza): Influence of endocrine glands on amount of water in striated muscle..582
Parkes, A. S.: Rôle of the corpus luteum in maintenance of pregnancy 409
— The functions of the corpus luteum. I. The mechanism of oestrus inhibition. II. The experimental production of placentomata in the mouse. III. The factors concerned in the development of the mammary gland 497
Patterson, Ellen: cf. King.....496
Paulian, D. (Aricesco): Clinical contribution to the study of myasthenia 403
Payne, W. B. (Van Peenan and Cartland): The distribution of the estrus producing and estrus inhibiting hormones in the ovary of the cow.....300
Payne, W. W. (Poulton): An unusual type of insulin reaction in a diabetic patient.....417
Pearl, F. V. (Brunn): Suprarenal apoplexy, bilateral 98
Peracchia, G. C.: On the function of prostate in relation to basal metabolism — experimental hyperprostatism 409
Perla, D.: cf. Marmorston-Gottesman 295
Perraud: cf. Porcherel.....498
Petit-Dutaillis, S.: cf. Kepinov....306
Pettinaria, V.: Greffe Ovarienne et Action Endocrine de l'Ovaire, Etude Histologique, Biologique, Clinique, et Chirurgical (Book Review) 575
Pfister, C. R.: Sex-proportion in children and the thyroid gland..300
Phear, A. G.: Addison's disease..218
Pierce, H. B.: cf. Murlin.....591
Pighini, G. (Colonna): Abortive action of liquor folliculi.....393
Plummer, C.: The therapeutics of an active orchitic extract.....300
Popov, P.: Adrenal secretion in angiostomized dogs 403
Porcherel, A. (Thevenot and Perraud): Notes on testicular grafts in sheep.....498
Porges, O.: cf. Adlersberg.....503
Poulton, E. P.: cf. Payne.....417
Powers, H. H. (Varley and Morrell): Assay of follicular hormone by vaginal administration.395
Pratt, G. P.: Tetany following thyroidectomy 229
Pratt, J. P. (Smeltzer): Nasal spray method of administering hormones of the ovary and pituitary gland 320
Preobrashensky, A. P. (Chernosatouska): Study on the antitryptic power of serum as a control of experimental athyreosis.....310
Pringle, G. L. K.: Endocrine imbalance and its reaction to chronic arthritis.....492
Ptaszrk, L.: Influence of sex hormones (male) on the basal metabolism in dogs.....498
— (Szuperski): Effect of diathermy of the thyroid gland on basal metabolism.....310
Ptschelina, Alexandra: Influence of blood from adrenal vein of rabbits before and after stimulation of splanchnic nerve on isolated intestine.....219
Puestow, C. B.: Primary pituitary tumors 589

Putnam, T. J. (Benedict and Teel): Studies in acromegaly. VIII. Experimental canine acromegaly produced by injection of anterior lobe pituitary extract.....589
Putschkow, N. W. (Krassnow): Influence of adrenals on urea-formation and barrier-formation of the liver.....98, 580

Raab, W.: Hormone und stoffwechsel (Book Review).....484
Rabinowitch, I. M.: An unusual case of diabetes and gout.....509
— Cholesterol content of blood plasma in diabetes mellitus..510
Radossaviyevitch, A. (Kostitch): Dysgenitalism of splenic origin.512
Rasmussen, A. T.: Histological evidences of colloid absorption directly by the blood vessels of pars anterior of the human hypophysis 103, 501
— Weight of principal components of the normal male adult human hypophysis cerebri.....103
Rathery, F. (Kourilsky and Gilbert): The action of the ovarian hormone on glycemia in normal dogs 496
Ravault, P. P. (Bouysset): Changes in the arterial vaso vasorum in the rabbit following intravenous injections of adrenin. The early microscopic changes in adrenin arterio-sclerosis 487
Ravier, J.: cf. Loeper.....508
Reed, C. I.: Carbohydrate metabolism in parathyroidectomized dogs 594
Regnier, J.: cf. Cardot.....514, 595
Reid, W. D. (Kenway): Electrocardiographic signs associated with low basal metabolism.....191
Reinhoff, W. F., Jr. (Lewis): Relation of hyperthyroidism to benign tumors of the thyroid gland.424
Reitzel, R. J. (Stone): Parathyroid extract—Collip—as a diuretic..106
Retterer, E.: Note on change in testicular grafts in he goats and rams 586
Reuterskiold, K.: cf. Andrews....503
Revue Belge des Sciences Medicales (Book Review).....573
Reye: Early clinical symptoms of disappearance of anterior lobe of pituitary.....414
Ricaldoni (Isola): Congenital and familial disease characterized by dystrophia adiposogenitalis with pigmented retina and polydactly.414
Richardson, H. B. (Loebel and Shorr): Respiratory metabolism of excised normal and diabetic tissue 418
Richter, C. P. (Brailey): Regulation of normal water-intake in rats and its experimental modification through brain punctures.583
Richter, C. P. (Wislocki): Activity studies on castrated male and female rats with testicular grafts, in correlation with histological studies of the grafts.....101
Riddle, Oscar: Endocrine regulation of reproduction.....311
— Some inter-relations of sexuality, reproduction and internal secretion 498
— Thyroid size in the sexes.....596
— (Flemion): Role of anterior pituitary in hastening sexual maturity in ring doves.....414
— (Tange): Action of ovarian and placental hormone in pigeon.410
Riegele, L.: Innervation of glomus caroticum in man.....405
Rigler, R. (Singer): Heart hormone 102
Robb, R. C.: Is pituitary secretion concerned in inheritance of body size? 589
Roberts, S. E.: Tetany following the use of cocaine and epinephrine in intranasal operations.....580
Robinson, S.: cf. Manning.....496
Rogoff, J. M. (Stewart): Functions of the adrenal glands.....580
Rosenstein, A.: Amblyopia recidive after operative removal of the ovaries 586
Rowe, Allan Winter: Differential diagnosis of endocrine disorders.327
— (Lawrence): Protocols of non-endocrine cases simulating endocrinopathies 263
— (McManus): Metabolism of galactose. VIII. Non-diabetic glycosurias 592
— cf. Lawrence, C. H.....1, 109
Rowe, L. W.: Studies of oxytocin and vasopressin: pressor action.205
Rydin, de H.: Effect of chlorophyll and thyroxin on body weight...519
— Effect of chlorophyll and thyroxin on the sensitiveness of the organism to reduced oxygen tension.....519

Sack, A. L.: cf. Zawadovsky.....230
Sainton, P. (Véran): Synthetic thyroxin 423
— — The experimental production of hoariness and alopecia areata in the rabbit by intensive and prolonged hyperthyroidization 519
Saito, S.: Effect of insulin administration upon the epinephrine content of the suprarenal body on rabbits.....488
— cf. Tachi.....488
Sajous, C. E. de M.: Rational endocrinology and organotherapy as foundation for getting efficiency in practice.....406
Saller, S.: Quantitative histological methods in testicular investigations 410

Sandiford, Irene: cf. Boothby....582
— cf. Deuel 227
Sandiford, Kathleen: cf. Deuel...227
Sanford, J. R.: cf. McClendon....310
Santenoise, D.: cf. Cardot...514, 595
Schazillo, B. A. (Ksendsowsky): The action of insulin on regeneration. The biological rôle of potassium and calcium ions in the process.....510
Scheps, M.: cf. Elmer.....224
Schlesinger, B.: Suprapituitary tumor? 501
Schlossman, H.: Thyroxin and nutrition 596
Schmidt, C. L. A.: cf. Goss.....299
Schoeller, W.: cf. Steinach.....499
Schönbauer, L. (Hogenauer): Clinical and experimental contributions to problem of testicular transplantation 410
Schteingart, M.: cf. Castex..305, 485
Schultz, W. H.: Quantitative study of human adrenals.....580
Schteingart, M.: cf. Castex.....587
Schwartzbach, S. (Uhlenhuth): Anterior lobe substance, the thyroid stimulator. IV. Effect in the absence of thyroid gland.....415
— cf. Uhlenhuth 415
Scott, W. J. M.: Influence of the adrenal glands on resistance. III. Susceptibility to histamine as a test of adrenal deficiency.....403
Scriver, W. de M.: cf. Lewis.....519
Searls, H. H. (Sharp): Endemic goiter in California.....520
Seckel, S.: Effect of thymus on water and salt regulation.....513
Sedallian, P.: cf. Mouriquand....579
Selle, R. M.: Thyroid-fed rats and high room temperatures.....423
Sellors, T. H.: Carotid body tumor.489
Selman, J. J. (Weinman): Observations on the effects of substances other than carbohydrate in relieving the toxic symptoms of insulin.....307
Sendrail, M.: Studies on sugar regulation by means of tolerance for insulin.....592
Sereisky, M. I.: Endocrine toxic epilepsy 596
Shapiro, S.: Endocrine disturbances among high school boys. I. Adiposo-dystrophia genitalis.144
Sharp, P.: cf. Searls.....520
Shepardson, H. C. (Anderson): Diabetic coma with marked hyperglycemia and recovery.....188
— cf. Lisser.....427
Shepardson, H. D. (Allen): Treatment of obstinate obesity.....492
Sherman, De W. H.: Exophthalmic goiter; report of two cases in children aged three and a half and six years.....423
Shookhoff, C.: The tachycardias..520
Short, J. J.: Increasing weight with insulin 307
Siddal, A. E.: Suggested test for pregnancy 410
Siebert, W. J.: Auto and homoiotransplantation of thyroid gland into brain of guinea pigs.....425
Siegmund, H. (Mahnert): The effect of infantile and foetal anterior lobe transplants on infantile gonads.....501
Silverus, Esther: cf. Thompson...597
Simond, A. E.: cf. Bugbee.....407
Simonetta, B.: On the internal secretions of salivary glands.....493
Simonnet, H.: cf. Brouha.....
.....221, 494, 500, 583
Simpson, Ethel D.: Effect of thyroidectomy on skeletal muscle in sheep 424
Simpson, Miriam E.: cf. Evans.500, 588
Singer, R.: cf. Rigler.....102
Sleeper, Francis H.: cf. Hoskins..
.....245, 459
Sloane, P.: cf. Kraus.....595
Smeltzer, Merrill: cf. Pratt.....320
Smith, P. E. (Engle): Experimental evidence regarding the rôle of the anterior pituitary in the development and regulation of the genital system.....501
Snell, A. M. (Rountree): Clinical experience with Addison's disease 581
Soiland, A. (Costolow and Meland): Radiation therapy in hyperthyroidism 520
Soskin, S. (Campbell): Utilization of carbohydrate by totally depancreatized dogs, receiving no insulin 592
Southam, A. H.: Ovarian sarcoma in a child associated with sexual precocity 498
Spatz, H.: On the influence of South Bavarian goiters on tadpoles and remarks on the technique 229
Spohr, C. (Moore): Study of pigment in Addison's disease..... 98
St. Draganesco: cf. Marinesco....303
Stefko, W. H.: Modification of endocrine glands following insufficient alimentation in man.....297
Steinach, E. (Dohrn, Schoeller, Hohlweg and Faure): The biological actions of the female sex hormone 499
— (Kun and Hohlweg): Reactivation of the senile ovary and of the female organism by hormonal methods.....101
— (Kun and Halhweg): Reactivation of senile ovary and the whole female organism by hormonal procedure 223

Stern, L. (Belkina and Zlatowierow): Influence of thyroidectomy and parathyroidectomy on the passage of material from blood to cerebro-spinal fluid....597
Stewart, G. N.: cf. Rogoff.....580
Stone, C. T.: cf. Reitzel.....106
Strauss, A. E.: Heart-black auricular flutter, and adenoma of thyroid 597
Stricker, P. (Grueter): Action of anterior lobe of hypophysis on milk secretion 589
Strouse, S. (Glassberg): Diabetes. Late results of insulin treatment. Treatment with synthalin.....510
Strugariu, S.: cf. Bacaloglu.....504
Sun, T. P.: The influence of suprarenal substance on muscle autolysis in vitro.....549
Sundberg, C. G.: Disappearance of adrenaline from circulating blood 404
Supernaw, J. S.: cf. Bast.....405
Sweeney, J. Shirley: Coexistent diabetes mellitus and diabetes insipidus with case report.....
Swingle, W. W.: Acid-base equilibrium after bilateral nephrectomy.219
Szent-Györgyl, A.: On the chemistry of the adrenal cortex.....581
Szuperski, M.: cf. Ptaszek.....310

Tachi, H. (Saito): Significance of the augmented epinephrine secretion after haemorrhage in dogs upon the simultaneous occurrence of hyperglycemia.....488
Takeuchi, S.: Insulin and metabolism of mineral salts.....307
Tange, M.: cf. Riddle.....410
Taylor, N. B. (Fine): Excretion of calcium through the intestine in parathyroidectomized animals...594
Teel, Harold M.: Effect of growth principle of hypophysis on female genital tract.....521
— (Watkins): Effect of extracts containing the growth principle of anterior hypophysis upon blood chemistry of dogs.589
— cf. Cushing 587
— cf. Putnam 589
Teitel-Bernard, A.: Hypodynamic heart condition and "heart hormone" 102
Télébakovitch, A.: cf. Kostitch...585
Thayer, S.: cf. Doisy.....583
Thevenot, J.: cf. Porcherel.....498
Thivolle, L.: cf. Fontes.....577
Thomas, H. M., Jr.: Nodular goiter with hyperthyroidism.....425
Thompson, G. P.: cf. Chidester..485
— cf. Eaton 485
Thompson, J. H.: Cress grown on adrenaline 404
— cf. Vincent 489
Thompson, Phebe K.: cf. Thompson 597
Thompson, W. O. (Brailey and Thompson): Effective range of iodine dosage in exophthalmic goiter: Preliminary report....597
— (Thompson, Silverus and Daily): Cerebrospinal fluid in myxedema 597
Timme, A. R.: Pancreatic cyst with diabetes 510
Timme, W.: Pluriglandular syndrome involving calcium deficiency and correlated with behavior disturbances 297
Tompkins, R. D.: Diabetes and tuberculosis 510
Tonnet, J.: cf. Loeper.....508
Torres, C. M. (de Azevedo): Lesions of the adrenal in yellow fever 488
Torres-Carreras, R.: cf. Cervera..181
Trimble, H. C.: cf. Maddock.....226
Trincao, C.: Note on the action of ergotamine on glycemia.....510
— cf. Fonseca 505
Troilo, E:. The action of adrenin and cholin on the blood pressure in decapsulated dogs.....488
Tucker, J.: Hyperthyroidism without visible or palpable goiter..230
Tuft, L.: Insulin hypersensitiveness; immunologic considerations and case reports.....105
Tung, P. C. (Chang and Ling): Hypophysis and urinary excretion of inorganic phosphate, sulphate and chloride.....104

Udenburg, A.: cf. Nemenow.....413
Uhlenhuth, E. (Schwartzbach): Anterior lobe substance, the thyroid stimulator. I. Induces precocious metamorphosis. II. Effect of feeding, anterior lobe upon amphibian metamorphosis. III. Effect of anterior lobe substance on thyroid gland.....415
— cf. Schwartzbach 415
Urechia, C. (Dragomir): Effect of ergotamin tartrate, adrenin, and atropine on the tension of the cerebrospinal fluid 296

Van De Walle, F.: Contribution to action of ovarian hormone.....301
Van Peenan, H.: cf. Payne.....300
Varé, P.: cf. Cardot.....595
Varga, V.: Insulin in treatment of pernicious anemia 593
Varley, J. R.: cf. Powers.....395
Véran, P.: cf. Sainton.....423
Velasquez, B. L.: Pharmacological studies on thyroxin.....598
Veler, C. D.: cf. Doisy.....583
Verda, D. J. (Burge and Green): Study of stimulating effect of testicular substance on sugar metabolism 46
Veran, P.: cf. Sainton.....519
Viale, G.: Pressure of adrenin and choline in lymph.....296

Viale, G.: Vagal function in adrenal insufficiency. Lack of vagal tonus.....488
— Vagal tonus, a function of circulating adrenin 582
— (Combes): Discharge of choline into the blood after injection of adrenin.....488
— (Kurie): Effect of thyroid-parathyroid apparatus on hyperthermia following injections of adrenin and of salt solution.594
Vidacovitch: cf. Cardot.....514
Vincent, S.: Function of the adrenal cortex 404
— (Thompson): Pneumin. A respiratory autocoid from the adrenal cortex discharged into the circulation via the lymphatics 489
Vogt, E.: Activation of insulin...418
— Ovarian cycle and insulin action 301
Von Euler, U. (Liljestrand): Effect of adrenalin on the minute volume of the heart.....405
Voss, H. E.: Functional heterotransplantation of endocrine glands 493
— cf. Loewe 496
Vye, M.: cf. Williams.....105

Wadehn, F.: cf. Glimm.....408
Waldenström, de J.: Effect of thyroxin on vagus excitability (electric) in frog's heart.....598
Walker, A.: Diabetes mellitus and pregnancy 227
Walker, B. S.: cf. Wyman.....581
Walker, T. T.: cf. Campos.....399
Walsh, E. L.: cf. Oldberg.....511
Wangensteen, O. H.: Blood supply of thyroid gland with special reference to vascular system of cretin goiter 598
Warfield, L. M.: Hypothyroidism.425
Warren, S.: cf. Page.....509
Warthin, A. S.: Constitutional entity of exophthalmic goiter and so-called toxic adenoma.....425
Wasti, H.: Influence of adrenalin and of some other internal secretions on contraction of mammalian skeletal muscle.....296
Watanabe, O.: cf. Hirohata.....108
Watarai, S.: cf. Hirohata.....108
Watkins, O.: cf. Teel.....589
Watrin, J. (Florentin): Comparative influence of insulin and thyroxin on endocrine glands.....583
Watson, E. M.: Some observations on effect of blueberry leaf extract in diabetic mellitus.....105
Weinman, S. F.: cf. Selman.....307
Wellbrock, William L. A.: Malignant adenoma of the parathyroid glands 285
von Wendt, G.: Biology of iodine and iodine combinations.....598
Werner, G.: Body changes following experimental castration.....587
— Studies on modifications of sugar, calcium, and urea in blood following experimental castration 587
Wertheimer, E.: cf. Abderhalden. 106, 513
Westedt, A.: Anthropometric investigations in acromegalics....415
Westman, A.: Concerning the primateship of the ovum.....499
Wheelon, H.: Geographical factors in calcium metabolism.....363
White, Priscilla: cf. Joslin.....507
Wieland, E.: Macrogënitosmia praecox in a 4½-year-old boy with carcinoma of the third ventrical and an intact pineal gland.411
Wiesli, P.: A method for early diagnosis of bitemporal hemianopsia in tumors of the pituitary.502
Wilckens, E.: cf. Lipschutz.....588
Wildebush, F.: cf. McClendon....585
Wilder, Russell M.: Hyperparathyroidism: Tumor of the parathyroid glands associated with osteitis fibrosa 231
— cf. Waltman.....593
Wiles, H.: cf. McClendon.....585
Williams, J. R. (Vye): Use of posters as a method of instruction in a diabetic clinic.....105
Wilkie, D.: The relation between concentration and action of adrenalin 296
de Winiwarter, H.: Histology of ectopic tests. Interstitial tissue and secretory phenomena.....499
Winkel, M.: Virilism (masculinity) in a case of adenoma of the suprarenal cortex 489
Winograd, A.: Hyperthyroidism in a 7-year-old girl.....426
Winters, H.: cf. Flexner.....517
Wishnofsky, M. (Frankel): Parathyroid extract and glucose tolerance in diabetes mellitus.....106
Wislocki, G. B.: cf. Richter.....101
Witschi, E.: Effect of high temperature on the gonads of frog larvae 223
Wolf, W.: New method for stimulation of endocrine glands with radium 493
Wolff, H. G.: Cerebral circulation. XI. Action of extract of posterior lobe of pituitary gland.....590
Wolman, I.: cf. Flexner.....517
Wolnar, A. O.: The rôle of secretin in the regulation of the alkali-reserve of the blood.....511
Waltman, H. W. (Wilder): Diabetes mellitus 593
Womack, N. A.: cf. Cole.....308
Worster-Drought, C.: Acromegaly; amyotrophic lateral sclerosis...502
— Acromegaly with unilateral paresis of 6th and 7th cranial nerves 415

Worster-Drought, C. (Archer): Case of dyspituitarism.....224
Wyllie, W. G.: Two cases of suprapituitary tumor (adamantinoma) 502
Wyman, L. E.: Cortical and medullary factors in suprarenal insufficiency 581
— Studies on suprarenal insufficiency. I. The effect of suprarenal insufficiency on reproduction and the oestrus cycle in the albino rat.....219
— (Walker): Studies on suprarenal insufficiency. IV. The blood sugar in suprarenalectomized rats 581

Yamashita, Y.: Experimental investigation of the internal secretion of the prostate.....300
Yang, C. S.: Influence of adrenalin on human spleen and blood picture 219

Zawadovsky, B. M. (Sack): Influence of thyroid on higher nerve function of dogs. I. Action of single doses of thyroid on conditioned reflexes under simple experimental conditions 230
Zerada, M.: The changes in the ovaries and other organs of animals injected with various ovarian substances.....499
Zimmerman, L. M.: Exophthalmos following operations for the relief of hyperthyroidism.....599
Zlatowierow, A. O.: cf. Stern.....597
Zondek, B.: Preparation of female sex hormone from urine, especially from urine of pregnant woman 101
— (Ascheim): Anterior lobe and ovary 503
— — Ovulation in pregnancy brought about by anterior pituitary hormone 503
— cf. Aschheim 405
Zunz, E. (La Barre): Note on the cause of the increased output of insulin following intravenous injection of non-hypotonic solution of secretin.....106
— — Response of the higher nervous centers to hypoglycemia following insulin.....511
— — The direct stimulation of the islands of Langerhans by adrenin 418

Subjects

Abortive action of liquor folliculi.393
Acromegalics, anthropometric investigations in 415
Acromegaly and Graves' disease..164
— — paresis 415
— case of 502
— experimental canine, and hypophysis extract 589
— genital hypertrophy and.....521
— pituitrin glycemic reaction in..564
Acterol and parathyroid tetany...227
Activation of insulin.....418
Addison's disease, case of.....218
— — clinical experience with....581
— — in negro 216
— — pigment in 98
Adenoma in Graves' disease.....164
— toxic, and exophthalmic goiter.425
Adrenal ablation and adrenal cortex feeding 217
— — — adrenin and choline in lymph 296
— — — basal metabolism.....406
— — — blood sugar 219
— — — cortical hormone.....401
— — — denervated spleen.....403
— — — lactic acid 218
— — — lowered temperature.....399
— — — metabolism 578
— — — — of rats.....399
— — — oestrous cycle 485
— — — respiratory failure 489
— — — urea-forming and barrier function of liver.....580
— — clinical studies of.....400
— — effect of, upon life of rabbits 579
— administration and number of erythrocytes 580
— and dementia praecox..... 73
— — blood pressure regulation...399
— — capacity for prolonged muscular work 399
— — compensatory changes in blood pressure 486
— — dementia praecox 491
— — exhaustion from lack of sleep 405
— — Graves' disease 164
— — Recklinghausen's disease...553
— — tubercular toxin 399
— cortex, action of tentanus toxin on 579
— — adenoma of 487
— — and gonads 216
— — — hypophysis 588
— — — medulla extract, influence of, on growth and maturity 485
— — — respiration 404
— — chemistry of 581
— — feeding and adrenal ablation.217
— — hormone of 401
— deficiency and histamine.....403
Adrenal, disease of, and melanin. 98
— — — metabolism and; case studies of..... 1
— extirpation and adrenine action on isolated intestine.....219
— — urea-formation and barrier-function of the liver..... 98
— extract, action of, on blood pressure in decapsulated dogs.488
— — and arterial blood pressure and blood flow.....577
— — — blood flow in skeletal muscle 578
— — — blood platelets 296
— — — carotid sinus.....578
— — — cerebrospinal fluid 296
— — — choline in adrenal.....488
— — — hyperglycemia 488
— — — hypotension in tabetics..216
— — — metabolism 579
— — — water content of striated muscle 582
— — influence of, on mammalian skeletal muscle 296
— — reaction and parathyroid medication 402
— functional insufficiency of.....217
— function of suprarenals on diphtheria intoxications.....403
— gland, functional activity of..577
— — functions of 580
— — immunologic studies in relation to 295
— — separation of new physiologically active principle of 578
— hemorrhage in new born infant 97
— in macrogenitosomia adiposa congenita 149
— — yellow fever 485
— insufficiency and vagal function 488
— — cortical and medullary factors 581
— lesions of, in yellow fever.....488
— mydriasis and menopause.....401
— obesity and; hirsutism and; pubertas praecox and.....149
— pathology and myasthenia.....403
— preparations, dual calorigenic activity of 402
— quantitative study of.....580
— reaction to morphine.....487
— secretion and pneumogastric nerves 402
— — following anastomosis of gland with carotid artery and jugular vein of another dog 401
— — in angiostomized dogs.....403
— secretory reaction in dogs with diphtheric intoxication 403
— substance and carbohydrate metabolism 416

Adrenal substance and muscle autolysis; as catalyst.....549
———— vegetable life 404
—— disappearance of, from circulating blood 404
—— effect of on adrenal secretion 402
— supposed existence of pro-adrenin in 295
— thyroid and nervous system, inter-relations of 98
— thyroid apparatus, fever, heat regulation and climate.....574
— tissue and lecithin.....485
— tumors 486
—— in children 97, 487
Adrenalin, see Adrenin.
Adrenin (or Adrenalin) and arterial vaso vasorum.....487
—— basal metabolism, calcium and potassium 485
—— blood sugar 507
—— isolated heart 216
—— muscle fatigue in adrenalectomy 295
—— pancreas 418
—— portal circulation 295
—— spleen 485
— concentration and action.....296
— effect on embryonic heart.....537
———— minute volume of heart..405
— failure of heart to respond to..215
— in adrenals in starvation 97
—— fever 577
— influence of, on spleen and blood picture 219
— like substance in heart.....487
— oral administration of..... 88
— subcutaneously injected in human subjects 98
Alopecia areata and thyroid.....107
Alveolar CO_2 in endocrine disorders 327
Amenorrhea, ovary in 299
Amino acid production catalyzed by adrenal 549
Anaemia, metabolism in.....109
— primary, simulating hypothyroidism 263
Anesthesia and thyroidectomy....517
— hypophysis hormones and placentoma reaction 500
— lobe and ovary.....503
—— extract and corpus luteum..583
———— injections and uterine change in mice.....588
— lobe injury and labor.....414
Anthropometric investigations in acromegalics 415
Antitryptic titre in pregnancy and hyperthyroidism 517
Arterio-sclerosis, adrenin 487
Arthritis, metabolism in.....109
Asthenia in adrenal disease..... 1
Asthma, metabolism in.....109
Atropine and thyroid.....228

Bacteria from goiter tissues; bacteriologic technic for their cultivation 309
Basal metabolism and adrenin....485
———— anterior lobe extract....587
———— diathermy of thyroid....310
———— electro-cardiograph 191
———— follicular hormone 300
———— male sex hormones.....498
———— oestrous cycle 100
———— pituitary substance 304
———— prostate 409
—— effect of ovarian preparations on 408, 496
—— in adrenal disease..... 1
———— dementia praecox 245
———— diseases of thyroid.....518
———— endocrine disorders 327
—— normal values of.....582
—— suprarenal and thyroid in relation to 406
Basedow's disease and iodized salt.421
Bio-assay of preparations of ovarian follicular hormone 407
Blood calcium and colectomy 511
———— spasmophilia; and geographical factors 363
— chemistry and anterior lobe extract 589
———— thyroid feeding 423
—— in endocrine disorders.....327
— count and long continued insulin administration 591
— glucose curve in diabetes.....104
— morphology and chemistry in adrenal disease 1
—— in endocrine disorders.....327
— pressure and insulin 591
———— pituitary extract ...205, 302
—— in endocrine disorders.....327
— sugar and adrenal ablation....219
———— ergotamine 505
———— extra pancreatic grafts ..591
———— hyperglycemia producing substance 306
———— hypophysis extracts 103
———— liver feeding 590
———— pancreatic grafts 591
———— pituitrin in pituitary disorders 564
———— sugar in urine in normals and diabetics 504
———— x-ray of pancreas.....225
—— blood changes and cell damage in kidney and liver after "glukhorment".....306
—— effect of insulin on fasting..104
—— in Graves' disease.....164
———— suprarenal ablation 581
—— insulin and adrenine action on 507
— supply of thyroid gland 598
Bone diseases and endocrine defects 484
—— metabolism in 109

Calcification in pituitary adenomas 455
Calcium, geographical distribution of, in Washington 363
— metabolism and geographical factors 363

Capons stimulated by testis extracts 367
Carbohydrate diet for hyperthyroidism 423
— metabolism 573
— — and sulfur action 416
— — — synthalin 504
— — in parathyroid ablation.....594
— — — parathyroidectomized dogs.594
— tolerance in juvenile diabetes..504
— utilization after pancreas ablation 592
Cardiorenal disease simulating hyperpituitarism 263
Carotid body tumor 489
— sinus and adrenin output.....578
Castration and gaseous metabolism 407
— — testicular grafts 101
— effects of counteracted by testis extracts 367
— in turkeys 220
— temporary, by ligation 494
Cholecystitis simulating dyspituitarism 263
Cholesterol content in blood plasma in diabetes mellitus.....510
Chromophobe adenoma of pituitary associated with gynecomastia...529
Chondrodysplasia simulating hypopituitarism 263
Chondrodystrophic dwarfs 303
Chronaxie of nerves and muscles in insulinized frogs.....509
Circulatory hormone, detection and action of 490
Colectomy and parathyroid tetany.511
Colloid content thyroid, iodine and 49
Constitution and internal secretions 484
Corpora lutea, histological studies of 408
Corpus luteum and anterior lobe extract 583
— — — follicular hormone 99
— — — folliculine, antagonism between 584
— — — oestrous cycle 221
— — — ova in transit.....499
— — — pregnancy 409
— — — sterility 100
— — — uterus reaction 222
— — effect of, on continuance of pregnancy 497
— — function of 497
— — injections and changes in ovary 499
— — physiology of 221
Cortex of adrenal hormone.....401
Cortical hormone and adrenal ablation 401

Dementia praecox, endocrine conditions in 73
Diabetes and accessory forms of treatment 504
— — diet 509
— — gout 509
— — hyperthyroidism..228, 467, 506
— — insulin 417
Diabetes and insulin resistance...417
— — pancreatic cyst 510
— — sensitiveness of higher nervous centers to sugar.....306
— — sympathetic affections 303
— — tuberculosis 510
— effects of guanidine derivatives in 305
— experimental studies of.....573
— hyperglycemia of 305
— in negroes 505
— insipidus and hypophysis.....102
— — — intranasal pituitary extract treatment 411
— — — nasal treatment of powdered pituitary lobe...412
— — — posterior pituitary 302
— — effect of insulin upon polyuria in 226
— — insulin and hypophysin action in 303
— — simulating endocrinopathy..263
— — with diabetes mellitus 477
— insulin and synthalin 510
— in twins 505
— — young adults 509
— insulin resistance in 507
— mellitus 593
— — and blueberry leaf extract..105
— — — growth in children.....505
— — — insulin treatment 506
— — — pregnancy 527
— — — synthalin 226
— — cholesterol content of blood plasma in 510
— — electrocardiographic studies of 305
— — latent tolerance in.....506
— — synthalin treatment in.....508
— — with diabetes insipidus.....477
— relative position of, as cause of death 417
— with ocular complications.....225
Diabetic children 507
— clinic, instruction in.....105
— coma and hyperglycemia.....188
— — insulin treatment of.....508
— therapy 305
— tissue, respiratory metabolism of 418
— treatment, present results and outlook of 416
Dementia praecox, endocrine studies in; metabolism in.....245
Diseases of endocrine glands.....574
— — the thyroid 575
Diuretic action of parathyroid extract 594
Duodenal ulcer simulating dyspituitarism 263
Dwarfism simulating hypopituitarism 263
Dystrophia adiposo-genitalis, case of 224
— — with pigmented retina and polydactly 414
— — with retinitis pigmentosa, mental deficiency and polydactylism 533

Dystrophia genitalis in Laurence-Biedl syndrome 375
Dystrophy, progressive muscular simulating endocrinopathy 263

Ear diseases, metabolism in.....109
Electrocardiograph, basal metabolism and myxedema 191
Endemic goiter 108
——— in Massachusetts 227
Endocrine defects, growth disturbances and bone diseases.....484
— diseases 213
— disorders, cases simulating....109
——— differential diagnosis of; complications of; presenting symptoms in; family histories in; personal histories in; fertility in; physical findings in; mental conditions in; laboratory findings in 327
— disturbances among high school boys 144
——— in infant and adolescent psychopathics 490
— factors in dementia praecox...491
— glands, and water content of striated muscle 582
——— comparative influence of insulin and thyroxin on....583
——— diseases of 574
——— following alimentation in man 297
——— functional heterotransplantation of endocrine glands..493
——— in dementia praecox..... 73
——— menopause and puberty....408
——— stimulation with radium....493
— imbalance and chronic arthritis.492
— regulation of reproduction....311
— stimulus of feather follicles in hen-feathered and cock-feathered Campine and Bantam males 299
— studies in dementia praecox...245
— system and status thymico-lymphaticus 513
— toxic epilepsy 596
Endocrines, alkaloids and permeability 491
— in tuberculosis 491
— poisons and muscle chemistry..491
Endocrinology and organotherapy, rational application of.....406
Endocrinopathies, non-endocrine cases simulating 263
— sedimentation time in.....406
Ephedrin, and intestine and bronchi 99
Epinephrine and hepatectomy....295
— content in suprarenals and insulin administration 488
— hemodynamic action of.....400
— injections in postoperative embolism and heart failure....487
— See also Adrenin.
Epididymis, hormone content of..367
Erythrocytes and adrenalin injections 580
Estrus producing and inhibiting hormones 300
Eunuchoidism, a case of.....413
— and dementia precox..... 73
Exophthalmic and toxic goiter, operative treatment of.....309
— goiter and toxic adenoma.....425
——— crises in 228
——— familial incident of.....228
——— in children 423
——— juvenile 108
——— iodine dosage in.....597
——— morphological change in, and Lugol's solution 108
——— treatment 517
Exophthalmos following operation for relief of hyperthyroidism...599
— Graves' disease without 164
Experimental overfeminizing 495
Eye diseases, metabolism in.....109

Female sex hormone...222, 408, 495
——— and breast development..406
——— biological action of.....499
——— in clinical cases..... 99
——— prepared from urine 101
Follicles, growth of 221
Follicular fluid injections and changes in ovary 499
— hormone and basal metabolism.300
——— corpus luteum 99
——— oestrous cycle 223
——— vaginal assay of.....395
Folliculine and corpus luteum, antagonism between 584
——— glycemia 496
——— insulin 494
——— uterus contraction 221
— from urine of pregnant women.583
Froelich's syndrome and roentgen-ray treatment 181
——— cases of in high school boys.144

Galactose metabolism.....592
— tolerance in adrenal disease... 1
Gall-bladder contraction and evacuation, hormone mechanism for..489
— hormone mechanism of.....220
Gaseous metabolism in castrated man 407
Gastric atony of nurslings and infants; therapeutic experiments with pituitrin in.....501
Gastro-intestinal tract, diseases in.109
Genital system regulation and hypophysis 501
Gigantism simulating hypopituitarism 263
Gland therapy, review of.....573
Glandular therapy and intelligence quotient 490
Glomus caroticum in man, innervation of 405
Glucose and insulin in diseases of children 417
— tolerance, findings in 1100 estimations of.....388
Glycemia and folliculine.....496
Glycogen after thyroidectomy, inanition 519

Goiter, and iodine in water.....310
— bacterial factor in.....309
— endemic, in California.....520
— Graves' disease without.....164
— in parents and the sex-proportion of children.....300
— nodular, and hyperthyroidism..425
— iodine and iodine combinations in.....598
— non-toxic, metabolism in.....109
— operations, deductions from....518
— prophylaxis with iodized salt..421
— simple 213, 575
— — treatment of.....484
— substance and growth.....229
— use of iodine in treatment of...519
Gonad ablation and hemolysins in blood 297
— — — hypophysis transplants...500
— — — sugar, calcium and urea in blood.....587
— — — thyroid immunization....297
— — — water content of striated muscle 582
— — body changes after.....587
— and adrenals.....149
— — adrenal cortex.....216
— — Graves' disease 164
— — high temperature.....223
— — Kurloff bodies.....298
— — Recklinghausen's disease...553
— disturbance and headaches.....220
— failure and dementia praecox..491
— infantile, and hypophysis transplants 501
— treatment in dementia praecox.245
— sex-specificity of.....100
Gout and diabetes.....509
Graves' disease and heart-block...514
— — pre-operative treatment of..107
— — types of.....164
Growth disturbances and endocrine defects 484
— pituitary and..... 63
— principle of hypophysis in acromegaly 521
Guanidine derivatives in diabetes..305
Gynecomastia associated with pituitary chromophobe adenoma....529

Handbuch der Inneren Sekretion..574
Heart diseases, metabolism in.....109
— embryonic, effect of adrenalin on.....537
— hormone 102
— rate and long continued insulin administration 591
Hebephrenia and thyroid treatment.459
Hermaphroditism, experimental...496
High carbohydrate diet in undernourished diabetics 503
Hirsutism and adrenals.....149
Histamine and pituitary extract assays 205
Hormones and inner secretions...213
— — metabolism 484
— in reactivation of ovary.....223
— of heart movement.....224
Hyperfunction of adrenal tissue...580
Hyperglycemia, action of insulin and ergotamine on.....510
— and adrenal extract.....488
— — medulliadrenal influence....215
— in diabetic coma.....188
— Numal and adrenin in.....577
Hypernephroma, case study..... 1
Hyperparathyroidism and osteitis fibrosa 231
Hyperthyroidism 426
— and benign tumors of thyroid gland 424
— — carbohydrate diet 423
— — diabetes.....228, 467, 506
— — exophthalmus 599
— — iodine 40, 107
— — joint conditions.....516
— — nodular goiter.....425
— — radiation 520
— antitryptic titre in.....517
— lymphocytosis in.....108
— thyroid ablation for.....516
— thyroidectomy for.....515
— without goiter.....230
Hypoglycemia and adenoma of islands of Langerhans.....417
— following insulin.....511
— spontaneous 503
Hypophyseal dwarfs.....303
— syndrome and morphological alterations of the rhinopharynx.102
Hypophysis ablation and kidney excretion of inorganic phosphate..104
— and adrenal cortex.....588
— — blood sugar.....564
— — colloid absorption by blood vessels 103
— — diabetes insipidus.....102
— — growth and reproductive processes 587
— — regulation and development of genital system.....501
— — sexual maturity in ring doves 414
— anterior and impairment of birth mechanism.....500
— — lobe extract and blood chemistry 589
— colloid in blood vessels of.....501
— disorder and mental disturbance.413
— eosinophil adenoma of and anthropometric investigations..415
— extract, action of, on urine output in diabetes insipidus....303
— — after thyroid ablation.....415
— — and basal metabolism.....587
— — — blood pressure.....302
— — — blood sugar.....103
— — — constipation 499
— — — diabetes insipidus.....411
— — — experimental canine acromegaly 589
— — — "Geographical skull"....499
— — — milk secretion.....589
— — — oestrus cycle.....102, 588
— — — proliferation of fibroblasts.302
— — — secretion into blood stream 587
— — — thyroid 415

Hypophysis extract in gastric atony of infants 500
— — mode of action of.....500
— — sex glands, sex function and growth 63
— hormone and ovulation in pregnancy 503
— — of anterior lobe in urine and diagnosis of pregnancy...405
— hormones in guinea pig.....303
— implants and ovary changes....588
— — — ovary stimulation 588
— — — sexual development.....298
— irradiation of.....222
— — in menstrual disorders.....584
— method for early diagnosis of tumors of.....502
— posterior lobe extract of, and cerebral circulation.....590
— powdered, in treatment of diabetes insipidus.....412
— radiotherapy of tumors of.....413
— Roentgen therapy in tumors of.411
— secretion and body size.....589
— stimulation with radium.....493
— transplants and gonadectomy..500
— — oestrous failure 496
— — effect of, on infantile gonads.501
— weight of main body of.....103
Hyposuprarenal and hypothyroidism 421
Hypothyroidism 425
— and basal metabolism 191
— — hyposuprarenalism 421
— juvenile 422
— with marked abdominal plethora and polycythemia 421

Impotence and pituitary tumor...429
Infantilism in Laurence-Biedl syndrome 375
Infra-red radiation and growth....308
Inner secretions in light of morphological research.....484
Insulin administration and epinephrin content.....488
— — long continued, effect of....591
— and bilateral ovarian ablation..586
— — blood pressure.....591
— — — sugar 507
— — capillary circulation.....225
— — diabetes 417
— — emaciation 305
— — ergotamine, action of, on hyperglycemia 510
— — folliculine 494
— — glucose, in diseases of children 417
— — mineral salts metabolism....307
— — ovulation 222
— — pancreas secretion.....505
— — pituitrin in diabetes insipidus.226
— — regeneration 510
— — thyroxin, comparative influence of, on endocrine glands 583
— — underweight 217
— — water content of striated muscle 582
— — weight increase.....307
Insulin action and ovarian cycle..301
— — of, on urine output in diabetes insipidus.....303
— — on perfused mammalian liver.504
— activation 418
— activity, inhibition of.....104
— effect on acetonuria.....505
— — — fasting blood sugar.....104
— hypersensitiveness 105
— hypoglycemia without symptoms 226
— in cases of impermeable kidney.508
— — diabetes insipidus 226
— — treatment of pernicious anemia 593
— injections and fatty atrophy...503
— — toxicosis of pregnancy.....105
— menorrhagia treated by.....407
— output and vagus section.....106
— pituitrin antagonism.....564
— postoperative dangers of.....503
— production 506
— relation of liver to action of....591
— resistance in a diabetic....417, 507
— tolerance and sugar regulation.592
— toxicity 307
— transmitted through placenta..592
— treatment and haematuria.....307
— — for subcutaneous fat in diabetic 505
— — in severe diabetes mellitus..506
— — of diabetic coma.....508
— — — scleroderma 509
— use in out-patient department..504
Insulinized frogs, chronaxie of nerves and muscles in.....509
Internal organs of selachians..... 97
— secretions and constitution.....484
— — — personality 484
— — comparative physiology of...213
— — of salivary glands.....493
— — sexuality and reproduction..498
Interrenin, suprarenal cortex hormone 486
Iodine and compensatory thyroid hypertrophy; colloid liquefaction 49
— — hyperthyroidism 107
— content in thyroid of cattle....517
— — of thyroid 514
— dosage in exophthalmic goiter..597
— effect on thyroid.....228
— in water, and goiter.....310
Iodized salt and goiter.....421
Islands of Langerhans and hypoglycemia 417

Juvenile diabetes, carbohydrate tolerance in.....504

Kidney diseases, metabolism in...109
— function in adrenal disease.... 1

Laurence-Biedl syndrome; two cases of; treatment of.....375
Laurence-Moon-Biedl syndrome...533
Lecithin and adrenal tissue.....485
Leukemia, myelogenous, simulating hyperthyroidism 263
Liquor folliculi, abortive action of.393
Liver and parathyroid.....511
— extract, standardization of.....415

Liver feeding and blood sugar...590
— relation of, to action of insulin.591
Lugol's solution and morphological changes in exophthalmic goiter..108
Lung volume in endocrine disorders 327

Macrogenitosomia adiposa congenita; adrenals in; heredity of; treatment of; obesity of.....149
— praecox with carcinoma of third ventricle and intact pineal...411
Macrosomia adiposa congenita; new syndrome 149
Male hormone 517
— — in urine 407
— sex hormones and basal metabolism 498
Malnutrition, metabolism in.....109
Mammary apparatus and placental hormone 499
— glands, development of.....497
Medulliadrenal influence in emotional hyperglycemia.....215
"Menformon," oral administration of.....585
Menopause and adrenaline mydriasis 401
— — chronic arthritis 492
— — endocrine glands.....408
— — ovarian extracts.....495, 496
— effect of ovarian preparations on.408
Menorrhagia treated with insulin.407
Menstrual disorders, irradiation of ovaries and hypophysis.....584
Menstruation and ovarian ablation in monkeys 298
— — ovulation 408
— — irradiation of ovaries and hypophysis 222
— in acromegaly.....521
— — adrenal disease..... 1
— irregularities of, controlled by ovarian, thyroid and pituitary hormones .....
Mental deficiency in Laurence-Biedl syndrome 375
Metabolic studies following administration of suprarenal extracts.579
Metabolism and hormones.....484
— — thermo-regulation after adrenal ablation.....578
— of galactose.....592
— — mineral salts and insulin...307
— — rats after adrenalectomy....399
— in adrenal disease..... 1
— — anaemia diseases.....109
— — arthritis 109
— — atrophic rhinitis.....109
— — bone diseases.....109
— — dementia precox 245
— — diseases of asthma.....109
— — — — ear 109
— — — — eye 109
— — — — gastro-intestinal tract.109
— — — — pelvis 109
— — — — skin 109
— — epilepsy 109
— — gall bladder infections.....109
— — gout 109
Metabolism in heart diseases.....109
— — kidney diseases 109
— — malnutrition 109
— — mental arrest.....109
— — miscellaneous nerve diseases.109
— — neuroses 109
— — obesity 109
— — paralysis agitans and Parkinson syndrome 109
— — primary focal infections....109
— — psychoneuroses 109
— — syphilis 109
— — tuberculosis 109
— — tumors 109
Mitosis, thyroid, iodine and..... 49
Mongolian idiocy, clinical study of.492
Monkey, reaction of, to follicular hormone 395
Muscle autolysis, adrenal as catalyst of.....549
Myogenic function of embryonic heart 537
Myxedema and basal metabolism..191
— — cerebrospinal fluid 597
— childhood, associated with Recklinghausen's disease.....553
— studies in.....422

Nephrosis, thyroid and parathyroid medication in.....519
Nerve diseases, miscellaneous, metabolism in.....109
Nervous system lesions, central, simulating hypothyroidism.....263
Neurofibromatosis with myxedema.553
Neuroses, metabolism in.....109
Non-diabetic glycosuria.....592

Obesity and adrenals.....149
— — endocrine therapy.....492
— in Laurence-Beidl syndrome....375
— metabolism in.....109
Oestrous and insulin injection....222
— — oral administration of "Menformon" 585
— — ripe follicle..... 99
— — spleen ablation.....512
— — suprarenal insufficiency 219
— — testis extract 494
— — vitamin A deficiency.....495
— cycle and basal metabolism....100
— — — corpus luteum.....221
— — — follicular hormone.....223
— — — hypophysis extract.....102
— — — long continued insulin administration 591
— — — ovarian grafts.....494
— — — — regeneration 497
— — — pineal spleen ablation....494
— — in adrenalectomized rats....485
— failure and hypophysis transplants 496
— hormone in urine of pregnant cows 496
— inhibition and corpus luteum...497
— producing hormones.....517
Oral administration of adrenalin.. 88
Osteitis fibrosa and hyperparathyroidism 231

Ovarian ablation and menstruation in monkeys....298
——— bilateral, and sensitivity to insulin....586
— and placental hormone action in pigeon....410
— cycle and insulin action....301
— dysfunction, clinical manifestations....296
— extract and artificial menopause.299
——— menopause....495
——— rat oestrus....100
— follicular hormone, bio-assay of preparations of....407
— hormone and menopause, amenorrhea and oligomenorrhea..301
——— in relation to women....585
——— yeast....408
— hypertrophy and anterior pituitary....500
— preparations, effect of, on menopause and basal metabolism..496
——— menopause and basal metabolism....408
——— oestrus and regeneration of ovaries and uterus....101
— regeneration and oestrous cycle.497
— sarcoma and sexual precocity...498
— therapy....409
——— in surgical menopause....296
— tissue feeding, growth and metamorphosis....497
— transplantation and sterility...100
Ovariectomy and duration of pregnancy....299
— regeneration and oestrous....497
Ovaries and dementia praecox.... 73
— irradiation of....222
——— in menstrual disorders...584
— preserved, transplantation of.. ....100, 101
— transplantation of and duration of pregnancy....299
Ovary ablation and blindness....586
— active materials of....493
— and anterior lobe....503
— changes, hypophyseal implants and hormones from urine of pregnant women....588
——— in, by various ovarian substances....499
— desiccated, transplantation of..585
— hypophysis and; in acromegaly.521
— in amenorrhea....299
— morphological and experimental studies of....573
— nasal application of hormone of.320
— reactivation of, by hormone procedure....223
— stimulation with radium....493
— thyroid tissue, tumors of....586
— transplantation....585
——— after preservation on ice....585
— transplants, autoplastic, homoplastic and heteroplastic....575
Ovo-testis function in spayed hens.494
Ovulation and menstruation....408
Oxytocic hormone and uterus contraction....221
Oxytocin....412

Paget's disease simulating hyperpituitarism....263
Pancreas ablation and utilization of carbohydrate....592
— activity during hibernation....304
— and adrenin....418
——— dementia praecox.... 73
——— metamorphosis in tadpoles..104
— carcinoma of....216
— endocrine function of....304
— extract, hypoglycemic action of, when given orally....306
— graft and transfusion of normal diabetic blood....306
——— and blood sugar....591
— irradiation, glycemia and glycosuria....225
— ligature of ducts of, and glygogen titer....225
— secretion and adrenal ablation..104
— stimulation of external and internal secretion of....225
Pancreatic ablation and fat and lipoid content of blood....226
— cyst and diabetes....510
— grafts and blood sugar....591
Parathormone and bone regeneration....106
Parathyroid....596
— ablation and carbohydrate metabolism....594
——— calcium excretion through intestine....594
——— passage of material from blood to cerebro-spinal fluid....597
——— rise in temperature follow adrenin....594
— adenoma and osteitis fibrosa...231
— and dementia precox.... 73
——— liver....511
——— thyroid, influence of, on inorganic salt metabolism..595
— extract and bone regeneration..419
——— glucose tolerance....106
——— as a diuretic....106
——— diuretic action of....594
——— preparation and assaying of.573
——— (Collip) and tetania parathyreopriva....427
——— in tetany following use of cocaine and epinephrine.580
— function, calcium metabolism and chronic pulmonary tuberculosis....593
— malignant adenoma of....285
— medication and adrenal reaction.402
——— in nephrosis....519
— osteitis fibrosa and; calcium and phosphate metabolism and; muscle tone and....231
— stimulation with radium....493
— tetany and acterol....227
——— colectomy....511
——— tissue changes....419
——— coagulation time in....419

Parathyroid tetany treated.....419
— therapy in schizophrenia.....593
— thymic masses in infants.....106
— tumors of 511
Paresis and acromegaly.....415
Parkinson syndrome simulating hyperthyroidism 263
Pathology of organs of internal secretion 574
Pelvis, diseases of, metabolism in..109
Personality and internal secretions.484
Physiological variations in secretion of insulin.....418
Pineal ablation and oestrous cycle.494
— and dementia precox..... 73
— body, endocrine function of....512
Pitocin, assay of.....205
— in diabetes insipidus.....477
Pitressin, assay of.....205
— in diabetes insipidus.....477
Pituitary, action of testis extracts on gonads.....100
— adenomas, calcification in.....455
— and alterations of nasal structures 102
— — dementia praecox 491
— — diabetes insipidus.....302
— — thyroid interrelation in metamorphosis 412
— anterior, and ovarian hypertrophy 500
— apparatus, histophysiological studies of.....484
— cachexia 412
— chromophobe adenoma of, associated with gynecomastia....529
— deficiency and treatment in dementia praecox 245
— disorders, pituitrin glycemic reaction in.....564
— disturbance and headache.....220
— extract, assay of.....205
— — glycemic reaction in diagnosis 564
— — hyperglycemic effect of.....302
— — in mongolian idiocy.....492
— — — pyelitis 103
— — water and salt excretion....411
— innervation of 302
— nasal application of hormone of.320
— posterior lobe principles of....412
— substance and basal metabolism.304
— tumors 589
Pituitrin and portal circulation...295
— assay of.....205
— in gastric atony of nurslings and infants 501
— insulin antogonism 564
Placental and ovarian hormone action in pigeon.....410
— hormone 499
— transmission of insulin from fetus to mother.....592
Placentoma reaction and anterior hypophysis hormones.....500
Placentomata, production of.....497
Pluriglandular syndrome involving calcium deficiency and correlated with behavior disturbances.....297
Pneumogastric nerves and adrenal secretion 402
Pre-diabetes, typical case of.....416
Pregnancy and chronic arthritis...492
— — corpus luteum.....409, 497
— — diabetes mellitus.....227
— — lactation, calcium and phosphorus balance in.....299
— antitryptic titre in.....517
— diagnosis by detection of hormone of anterior lobe of hypophysis 405
— hormonal test for.....494
— in guinea pigs after ovariectomy 299
— ovulation in, brought about by pituitary hormone 503
— pituitary and..... 63
— suggested test for.....410
Pressor action of pituitary extracts.205
Prostate and basal metabolism....409
— — other endocrines.....300
— internal secretion of.....300
Pseudohermaphroditism 496
Psoriasis, thymus gland irradiation in.....512
Pubertas precox and adrenals....149
Puberty and endocrine glands....408
Pulse in endocrine disorders.....327

Quantitative histological methods in testicular investigations.....410

Radiation and hyperthyroidism...520
Radio therapy of tumors of hypophysis 413
Recklinghausen's disease; etiology of; manifestations of; endocrine relations of; treatment of.....553
Regeneration, insulin and Ca and K ions.....510
Rejuvenation process, review of work on.....408
Reproduction, endocrine regulation of.....311
— sexuality and internal secretion.498
Respiration in endocrine disorders.327
— and adrenal cortex.....404
Respiratory metabolism of excised normal and diabetic tissue.....418
Retinitis pigmentosa in Laurence-Beidl syndrome.....375
Rhinitis, atrophic, metabolism in..109
Roentgen rays in thyroid function.514
— therapy in hypophyseal tumors.411

Schizophrenia, endocrine studies in; metabolism in.....245
Scleroderma treated by insulin...509
Secretin and the alkali-reserve...511
— chemistry and physiology of...297
Sex characters of capons after injection of bull serum.....583
— function in adrenal disease.... 1
— glands and functions and hypophysis extract..... 63
— — antagonism of.....496
— hormones, chemical behavior of.584
— proportion in children and the thyroid gland of parents....300

Sex specificity of internal secretion of....100
Sexual development and hypophysis implants....298
— maturity in ring doves....414
— precocity and ovarian sarcoma.498
Sexuality, reproduction and internal secretion....498
Simple goiter....213, 575
Skin diseases, metabolism in....109
Spasmophilia and blood calcium...363
Spermatogenesis 99
— and x-radiation....495
Spleen ablation and blood platelets.296
— — — hemolysins in blood....297
— — — oestrous cycle....494
— — — sex cycle....512
— — — typhoid immunization....297
— and adrenin....485
Status lymphaticus, review of....513
— thymicolymphaticus 420
— thymico-lymphaticus and endocrine system....513
Sterility and infra-red rays.... 93
Sugar metabolism and testicular substance 46
— regulation and tolerance for insulin 592
— tolerance in endocrine disorders.327
Suprapituitary tumors....501
— — two cases of....502
Suprarenal apoplexy, bilateral.... 98
— blastomata 486
— carcinoma of....218
— cortex and virilism....489
— — hormone of....486
— insufficiency and the oestrus cycle 219
— renal heterotopia....215
Sympathetic ablation, clinical studies of....400
Sympatheticotonic type of Graves' disease 164
Syndactylism in Laurence-Biedl syndrome 375
Snydrome-complex, Ménière....406
Synthalin 510
— and carbohydrate metabolism..504
— — diabetes 510
— in treatment of diabetes mellitus 508
Syphilis, hereditary, and infant and adolescent psychophopathies....490
— metabolism in....109
— simulating dyspituitarism....263

Tachycardias 520
Temperature in endocrine disorders 327
Testes and dementia precox.... 73
— — thyroid 298
— destruction of nerve supply to.. 99
— ectopic, histology of....499
— extract and chronic ulcers of legs 408
— — — oestrous 494
— — correct effects of castration..367
— — preparation of; hormone effects of; assay of....367
Testes extracts, therapeutics of...300
— quantitative histological methods in investigations of....410
— stimulation with radium....493
— transplants 495
Testicle transplantation, clinical and experimental contributions to problem of....410
Testicular grafts, changes in....586
— — in castrates....101
— — — sheep 498
— hormone source of....409
— substance and sugar metabolism 46
Tetania parathyreopriva and parathyroid extract (Collip)....427
Thymus ablation and water content of striated muscle....582
— an intensive study of....419
— and Graves' disease....164
— — x-ray 512
— diagnosis and treatment of....420
— extract and water elimination..513
— — in mongolian idiocy....492
— gland irradiation....512
— vogue 512
Thyroid 596
— ablation and antitrypase in serum of normal sheep....310
— — and auricular flutter....597
— — — basal metabolism 406
— — — conditioned reflexes....107
— — — follow-up study 422
— — — hemolysins in blood....297
— — — hypophysis extract 415
— — — passage of material from blood to cerebro-spinal fluid 597
— — — skeletal muscle....424
— — — tetany 228, 229
— — — typhoid immunization....297
— — — water content of striated muscle 582
— — complications of....515
— — for hyperthyroidism....516
— adenoma and cancer of....309
— adrenals and nervous system, inter-relation of.... 98
— adrenal apparatus, fever, heat regulation and climate....574
— and atropine....228
— — cell division rate....308
— — cerebral irritability....595
— — compensatory thyroid hypertrophy 49
— — conditioned reflexes....230
— — dementia precox....73, 491
— — epilepsy 596
— — exhaustion from lack of sleep 405
— — hypophysis extract....415
— — infections 308
— — parathyroid, influence of, on inorganic salt metabolism.595
— — pituitary interrelation in metamorphosis 412
— — plumage growth....515
— — obesity 492
— — Recklinghausen's disease...553

Thyroid and synthetic thyroxin...420
——testes 298
——tubercular toxin.....397
——vagus 514
—basal metabolism in diseases of.518
—benign tumors of, and hyperthyroidism 424
—blood supply of.....598
—deficiency and treatment in dementia praecox.....245
—diathermy of, and basal metabolism 310
—diseases 575
——visceral projection reflexes..422
—disorder, distinction between metabolic and nervous symptoms in.....595
—disturbance and headache.....220
—dysfunction and recovery from exercise 107
—extract and nutrition.....596
———reduced oxygen tension..519
———synthetic thyroxin.....423
——cardiac and vascular nerve..516
——in mongolian idiocy.....492
—feeding and feathering in fowls.308
———metamorphosis in tadpoles 104
—function and myocardial disturbances 107
———roentgen rays 514
—functional activity of fetal.....422
—gland and tryptophan.....515
——effect of iodine and thyroid feeding on.....228
——hypertrophy and infra-red radiation 308
——life curve in goiter and goiter free territory.....310
——of parents and the sex-proportion of children.....300
—hormone in hyperthyroidism...514
—hyperplasia and function..... 40
—in menstrual disorders.....320
—iodine content of.....514
———in cattle 517
—mechanism of secretion in.....309
—medication in nephrosis.....519
—metastasis to, from endothelial myeloma of bone.....515
—neoplasm of.....420
—size in sexes.....596
—stimulation with radium.....493
—substance, fed to rats, and high room temperature.....423
—surgery and ablation.....574
—therapy in childhood.....422
—tissue tumors of ovary.....586
—toxemia and thyroid ablation...597
—treatment, and hoariness and alopecia areata in rabbit.....519
——in hebephrenic dementia praecox 459
——of alopecia areata.....107
—transplants 425
Thyroidal type of Graves' disease..164
Thyroidectomy and anesthesia....517
Thyroidectomy for hyperthyroidism 515
—inanition and glycogen.....519
Thyro-parathyroid ablation and rise in temperature following adrenin 594
———thyroid feeding 423
——influence of blood, blood serum and milk.....596
Thyro-parathyroidectomy, tetany, and blood calcium.....309
Thyroneural dystrophy.....595
Thyrotoxicosis and chorea minor..518
——tachycardias 520
—intracutaneous salt-solution test in.....519
—pathologic physiology of.....422
Thyroxine 574
—and body weight.....519
——heat regulation 106
——insulin, comparative influence of, on endocrine glands...583
——nitrogen metabolism 227
—pharmacology of.....598
—in the organism.....513
—pharmacological synthetic experiments on.....309
—synthetic, and thyroid extract..423
——effect of, on normal thyroid.420
Tinnitus arium; incidence of, in endocrine disorders.....490
Tryptophan and thyroid gland....515
Tuberculosis and diabetes.....510
—metabolism in.....109
—pulmonary, simulating hyperthyroidism 263
Tumors, metabolism in.....109

Urine chemistry in adrenal disease 1
———endocrine disorders.....327
Uterus contraction and hormone..221
—hypophysis and; in acromegaly.521
—reaction and corpus luteum....222
—subinvolution, hypoplasia and hormones 320

Vagal tonus and adrenin.....582
Vaginal, cyclic, changes in spayed animals 585
Vagotonic type of Graves' disease.164
Vagus and adrenal insufficiency...488
——thyroid 514
—stimulation and thyroid extract.598
Vasoligation and changes in hair..406
Vasopressin 412
—assay of.....205
Vegetative nervous system, hypercholesterolemia and arteriosclerosis 220
Virilism and adenoma of suprarenal cortex.....489
Vitamin A deficiency and oestrus..495

Water-intake in rats, regulation of.583
Weight in endocrine disorders....327

x-radiation and spermatogenesis..495
x-ray and thymus.....512

BOTH Vitamins Definitely Measured

HOW can vitamins be "measured?" What is meant by "standardized" when applied to Cod-liver Oil?

To test for *vitamin A potency* the oil is given orally to young albino rats which have been fed on a diet free from vitamin A. We ascertain how much oil is needed daily to correct the induced typical eye condition (xerophthalmia) and to institute a specified rate of growth.

Every lot of Parke-Davis Standardized Cod-liver Oil must contain not less than 13,500 units of vitamin A in each fluid ounce.

In determining *vitamin D potency* we use our quantitative adaptation of the "line test" technique of McCollum, Simmonds, Shipley, and Park. The oil is fed to young rats in which rickets has been induced. Each fluid ounce of Parke-Davis Standardized Cod-liver Oil contains not less than 3000 vitamin D units.

Parke, Davis & Company was the first commercial laboratory to express in units the potency of both vitamins A and D. Parke-Davis Standardized Cod-liver Oil is backed by years of research work in various phases of nutrition chemistry.

Quite aside from its vitamin richness, this product has other distinguishing features which will appeal to you. It is clear, bland, and as nearly tasteless and odorless as a pure Cod-liver Oil can be. May we suggest that in prescribing Cod-liver Oil for your patients you specify the Parke-Davis product?

Send for stock package

To any physician who is personally unacquainted with Parke-Davis Standardized Cod-liver Oil we will gladly send a 4-ounce bottle for free trial.

PARKE, DAVIS & CO.
WALKERVILLE, ONTARIO

WINNIPEG, MANITOBA MONTREAL, QUEBEC

PARKE-DAVIS STANDARDIZED COD-LIVER OIL

Armour's Elixir of Enzymes
is potent and palatable

Armour's vast sources of raw material, together with superior facilities for exact manufacture has given the medical profession an excellent product in "Elixir of Enzymes." It is particularly desirable as a stomachic stimulant and mild caraminative. It is useful in correcting faulty proteid digestions, and acts as a splendid vehicle for exhibiting iodids, bromide, salicylates and other drugs that disturb the digestive functions.

The rapid development of organotherapy has been one of the high-lights in the progress of modern medicine. And Armour has made it possible for the doctor to obtain these glandular products in convenient and absolutely standardized forms.

For more than thirty years, the Armour Laboratory has anticipated the needs of the medical profession in this highly specialized field. Rightly, it has earned the name of "*headquarters for medical supplies of animal origin.*"

Doctors all over the world regard the Armour label on organotherapeutic products as a symbol of confidence and reliability. You can inhesitatingly depend upon these Armour products: Thyroid, Pituitary preparations, Suprarenalin Solution, Concentrated Liver Extract, Corpus Luteum, Ovarian Substance and the various digestive Enzymes.

ARMOUR AND COMPANY

Chicago

PHARMACEUTICAL PRODUCTS